Electrophysiology of Oculomotor Delayed Response Tasks: A Model for the Maturation of Visual-Spatial Working Memory Networks

Carleigh Sanderson, Bachelor of Arts (Honours)

Child and Youth Studies

Submitted in partial fulfillment

of the requirements for the degree of

Master of Arts

Faculty of Social Sciences, Brock University

St. Catharines, Ontario

Acknowledgements

First and foremost, I want to thank Dr. Ayda Tekok-Kilic for her dedication to my thesis and for introducing me to the field of electrophysiology and ERP research. This work would not have come to fruition without her guidance and support, and I will be forever grateful that she pushed me right to the end. I would also like to thank my committee members, Dr. Tony Volk and Dr. Jan Frijters for their insight, and Dr. Valerie Shafer for agreeing to be my external reader. Their suggestions and feedback helped me to better understand my own research. Furthermore, I would like to thank Dr. Christine Tardif-Williams for her re-assurance throughout the process of completing my thesis, and I would especially like to thank Dr. Dawn Zinga for first sparking my interest in research during my undergraduate thesis. Moreover, I would like to thank my family (Mom, Dad, Michael Sanderson, Gregory Sanderson, Carissa Boyko-Sanderson, Alysha Coates and everyone else) for reminding me about the important things in life, and for supporting me as I pursue my academic goals. There are many other individuals that I would like to mention, so I will conclude this acknowledgement page with a quote that reflects my gratitude for all the support I have received during my time at Brock.

"Cultivate the habit of being grateful for every good thing that comes to you, and to give thanks continuously. And because all things have contributed to your advancement, you should include all things in your gratitude." -Ralph Waldo Emerson

Abstract

In the literature, persistent neural activity over frontal and parietal areas during the delay period of oculomotor delayed response (ODR) tasks has been interpreted as an active representation of task relevant information and response preparation. Following a recent ERP study (Tekok-Kilic, Tays, & Tkach, 2011) that reported task related slow wave differences over frontal and parietal sites during the delay periods of three ODR tasks, the present investigation explored developmental differences in young adults and adolescents during the same ODR tasks using 128-channel dense electrode array methodology and source localization. This exploratory study showed that neural functioning underlying visual-spatial WM differed between age groups in the Match condition. More specifically, this difference is localized anteriorly during the late delay period. Given the protracted maturation of the frontal lobes, the observed variation at the frontal site may indicate that adolescents and young adults may recruit frontal-parietal resources differently.

Table of Contents

List of Tables

List of Figures

List of Appendices

CHAPTER I

Introduction

Working memory (WM) is a fundamental cognitive process supported by the activation of distributed neural networks. In that sense WM is not accommodated by one or two neural structures but it is an "emergent property" of the brain (Postle, 2006 pp. 23). Cognitive and neurophysiological approaches to WM differ in terms of their level of conceptualization and complexity, although they all define WM as a dynamic system that holds information for a brief period of time in the absence of the information (i.e. stimulus) to be used in achieving prospective goal related behavior.

In the present study I adopt Fuster's neurophysiological model of WM, termed as the perception-action model (Fuster, 1985). According to his model: "WM mediates the logical and behavioural cross temporal contingencies between perception and action" (Fuster & Bressler, 2012, p. 211). A broad explanation of the model is that WM becomes activated once a mediation of sensory and frontal brain regions occur (Fuster & Bressler, 2012). Mediation of brain regions occurs when two or more structures become engaged to perform a cognitive function. The communication between brain regions is the premise for understanding how the brain is a network of neural function. Fuster (1985) states a clear distinction in the neural definitions of long term memory (LTM) and WM. The difference in the two networks is the persistent and recurrent activation of the WM network during tasks requiring goal-directed performance. Fuster's proposed temporal contingency has been frequently studied in simple but well structured paradigms called Delayed Response (DR) tasks especially in relation to visual-spatial WM.

DR tasks are the ultimate paradigms to investigate neurophysiology of WM because of their elicitation of persistent and recurrent activation of the frontal-parietal network (Funahashi,

2006; Fuster, 1985; Scherf, Sweeney, & Luna, 2006). The mediation of the frontal and parietal areas engages perceptual and action-based mechanisms in pursuit of goal directed behaviours (Fuster, 1985; Fuster & Bressler, 2012). DR tasks require the mediation of the frontal-parietal network to sustain retrospective codes (memory about an item or location) and prospective codes (action plans) (Constantinidis & Wang, 2004). The memory function of the frontal-parietal networks subserving WM is located in the pre-frontal cortex, and perceptual mechanisms are supported in the parietal areas (Fuster & Alexander, 1971; Srimal & Curtis, 2008). The cross-temporal mediation generates the necessary physiological and cognitive function required in WM (Fuster, 1985).

Oculomotor delayed response (ODR) paradigms belong to the family of DR tasks and elicit the frontal-parietal network in support of visual-spatial WM function. Classical ODR tasks measure the capacity to hold task-relevant information (i.e. location) in mind for a short period of time and use that information to execute a response (saccade) (Srimal & Curtis, 2008). To perform the task an individual is required to retain the location of a stimulus that appears for a few seconds and then disappears. An accurate response occurs when an individual directly gazes at the correct location retained in memory.

Delay period phases of ODR tasks require an active maintenance of stimulus location to prepare for a subsequent saccadic response (Fuster & Alexander, 1971; Serences, Ester, Vogel, & Awh, 2009; Sobotka, Dilltz, & Ringo, 2005). A particular focus of interest has been on the persistent neural activity observed in frontal and parietal areas during the delay period (Fuster & Alexander, 1971; Srimal & Curtis, 2008). The parietal lobe supports the basic sensory processes associated with oculomotor function, and the frontal regions support advanced cognitive function, such as memory (Postle, 2006). The integration of frontal-parietal structures supports

the early processing of sensory information and the subsequent oculomotor responses (Jung & Haier, 2007). More specifically, the frontal-parietal regions elicit motor planning such as direction of eye gaze in the generation of a saccadic response (Constantinidis & Wang, 2004).

The physiological and cognitive functions elicited in ODR tasks have been used to explore developmental differences of neural networks underlying visual-spatial WM. Given that the frontal brain regions are last to reach full maturation, the frontal and parietal activation in ODR tasks provide a model to explore developmental influences on neural network processes and function (Scherf et al, 2006). A breadth of research exists on the neural networks subserving visual-spatial WM (Klingberg, 2006; Srimal& Curtis, 2008).

Furthermore, a multitude of neuroimaging methods are used in investigations of the visual-spatial WM network. In corroboration of research results (Brigani, Bortelleto, Miniussi, & Maioli, 2010; Curtis, Rao, & D'Esposito, 2004; Singh, Kim, & Singh, 2003), the frontal-parietal network has become a known substrate involved in visual-spatial WM. Electroencephalography (EEG) is one of the techniques used in research. The EEG technique captures high temporal resolution of a large population of firing neurons involved in network function (Light et al., 2010). The high temporal resolution supports the investigation of neural activity at the level of milliseconds (Light et al., 2010). The timing and regional activations are captured with a dense electrode array. The electrodes are placed on the scalp to capture the activity of synchronously firing neurons that correlate to specific cognitive functions.

The neural activity captured with EEG can be evoked with paradigms using event-related potentials (ERPs). The ERP paradigm presents a target stimulus that is used as a reference point to observe subsequent task-related neural processes (Light et al., 2010). Compared to other brain imaging techniques, EEG provides a precise temporal timing of neural events, although it is

weak in its spatial resolution (Luck, 2005). However, technical advancements in the statistical processing of EEG data have allowed for source localization of network function (see Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002).

The current study explored developmental differences in the slow wave activity associated with activation of the frontal-parietal network in ODR tasks. Previous studies have suggested that activations of neural networks supporting WM function become more efficient as cortical regions mature and myelinate (Constantinidis & Wang, 2004; Scherf et al., 2006). The activation of the frontal-parietal network in ODR tasks provides a model to explore differences in the sensory and cognitive functions that support visual-spatial WM. Given that the notion of WM has evolved from a component-based model (Baddeley & Hitch, 1974), more investigations of the neural networks that underlie its function are needed. In viewing the brain as a neural network, it becomes necessary to understand how the recruitment of cortical regions subserving cognitive function change as the brain develops. In a recent ERP study with healthy young adults, Tekok-Kilic et al. (2011) reported task-related slow wave differences over frontal and parietal sites during the delay period of three ODR tasks. In the current study, I compared task-related slow wave activity in young adults (18-34 years) and adolescents (14-17 years) during the delay period of three ODRs. The goal of this EEG study was to use the well-defined oculomotor system to explore patterns of frontal-parietal visual-spatial WM networks in young adults and adolescents. In conjunction with slow wave data analysis, sLORETA was utilized to explore developmental differences in the regional activation of the frontal-parietal network involved in visual-spatial WM function.

For the purpose of this research it is critical to operationally define the function and mechanism of WM, as investigations are supported in different research traditions. Given the

physiological methodology used in this study, I adopted the definition of WM first proposed by researchers such as Jacobsen (1936), Fuster (1973), and Goldman-Rakic (1987). As such, I explored the activation of cortical networks during brief periods of memory retention. In keeping with traditional definitions, memory retention is the active maintenance of information in the absence of external prompts or cues (Fuster, 1973; Goldman-Rakic, 1987; Jacobsen, 1936). These operational definitions are complementary to the ODR methodology utilized in this study.

CHAPTER II

Literature Review

Working Memory: Cognitive and Physiological Approaches

Working memory (WM) is a cognitive processing system that actively holds and manipulates information during a short period of time (Baddeley & Hitch, 1974). Several models are proposed to explain WM (see Shah & Miyake, 1999). In one of the most influential WM models, Baddeley and Hitch (1974) defined WM as a multi-component, dynamic short-term memory system with three subunits that are responsible for retention of verbal and non-verbal (visual-spatial) information for the execution of goal-related behaviours (Baddeley, 2003; Postle, 2006). The two storage systems are called phonological loop and visual-spatial sketch pad. The phonological loop is responsible for maintaining auditory-linguistic based information through a process called articulatory rehearsal. The visual-spatial sketch pad holds and manipulates visual-spatial representations, such as in the mental rotations of images (Baddeley& Hitch, 1974; Baddeley, 2003). The third component is called central executive and it has been associated with attentional control. Central executive is implicated in the control of behavioural responses, and in the re-attainment of attention if interference occurs (Baddeley, 2003; Postle, 2006). Later, Baddeley (2000) added another component, called the episodic buffer, to the original WM model (Baddeley & Hitch, 1974). The episodic buffer is conceptualized as a connection between the two information-specific processing systems, and its functional purpose is to integrate incoming information held in WM with information held in long term memory. The integration of the memory systems provides a more coherent representation of the information to which an individual is attending (Baddeley, 2000).

As proposed by Funahashi (2006), "One way to understand how working memory is performed in the brain is to elucidate neural processes to achieve the active maintenance of information in the nervous system, to perform dynamic information processing, and to integrate different operations occurring in different brain areas," (p. 251). In corroboration of this, Baddeley and Hitch's (1974) WM model has been consistently substantiated by neuroimaging studies. Several studies have reported anatomical separation in the neural responses when individuals are required to perform verbal or visual-spatial WM tasks (Cornoldi & Vecchi, 2003; Hönegger et al., 2011; Smith, Jonides, Marshuetz, & Koeppe, 1998; Thomason et al., 2009; Zollig, Martin, & Kliegel, 2010).

However, the literature contends that results are too ambiguous to state that specific information processing systems correspond to one cortical region in the brain (Baddeley, 2003; Cornoldi & Vecchi, 2003; Postle, 2006). For example, according to Postle (2006), WM is an emergent property that relies on functional connectivity between regions. Furthermore, he contends that WM is not domain-specific, but rather a general cognitive function closely associated with attentional control. Interestingly, the distinct pattern of neural activation in visual-spatial WM is not clearly understood, especially when compared to the phonological loop (Cornoldi & Vecchi, 2003). Despite the uncertainty about how neural pathways function in visual-spatial WM, the multi-component WM system does provide a strong theoretical model to represent how specific types of information are held in memory for execution of a behavioural response (Baddeley, 2003).

Given the current inconsistency among research findings surrounding neural networks supporting visual-spatial WM, much effort has been put forth in physiological studies to investigate the cortical mechanisms involved in its function (Constantinidis & Wang, 2004).

Knowledge about the physiology underlying WM began to emerge in 1920s, with Hunter's introduction of delayed response tasks (Hunter, 1913). During a delayed response (DR) paradigm stimulus presentation is followed by a brief delay in which the participant must hold the task relevant information in mind (Constantinidis & Wang, 2004). Hunter (1913) hypothesized that the delay period before response execution activates short term memory to retain the task relevant information, (i.e. both the identity of the stimulus and the goal related action plans).

Subsequent research with monkeys supported Hunter's (1913) hypothesis of STM activation during the delay period in DR paradigms (Goldman-Rakic, 1987, 1998; Jacobsen, 1936). From this knowledge, the physiological framework underlying working memory function began to evolve. The first neural investigations of WM were done with monkeys who had lesions on the prefrontal cortex (Jacobsen, 1936). Similarly, in an electrophysiological study with monkeys, Fuster (1971) discovered a sustained activation of memory cells in the prefrontal cortex. Goldman-Rakic (1987) proposed the dorsolateral prefrontal cortex (dLPFC), a structure within the prefrontal cortex, was a critical substrate to understanding WM. The dLPFC is a neural structure that supports motor planning, organization, behavioural regulation and has been closely associated with WM function (Johnson & de Haan, 2011).

Fuster (1971), Goldman-Rakic (1987) and Jacobsen's (1936) early research spurred scientific inquiry into the cognitive and neural components subserving visual-spatial WM function. In considering Goldman-Rakic's (1987) findings, the dLPFC has been extensively examined to better understand WM (Funahshi, 2006). Fuster's discovery of elevated and persistent neural activity during the few seconds between the presentation of sensory information and the subsequent response has since been regarded as a neural correlate of information maintenance (Funahashi, 2006; Scherf, Sweeney, & Luna, 2006). Considering the knowledge

that WM is reliant upon the intact prefrontal cortex in general, recent studies have since examined prefrontal activations subserving memory retention (Curtis, Rao & D'Esposito, 2004; Scherf et al., 2006; Srimal & Curtis, 2008).

As stated above, different research traditions have been used to investigate WM, and thus it is critical to operationally define the function and mechanisms of WM for the current study. Given the physiological methodology used in this study, I adopted the definition of WM first proposed by researchers such as Jacobsen (1936), Fuster (1973), and Goldman-Rakic (1987). As such, I explored the activation of cortical networks during brief periods of memory retention. In keeping with traditional definitions, memory retention is the active maintenance of information in the absence of external prompts or cues. These operational definitions are complementary to oculomotor delayed response task (ODR) methodology.

Oculomotor Delayed Response Tasks (ODR)

The ODR paradigm belongs to the family of Delayed Response (DR) Tasks. The ODR task has been accepted as a gold standard research paradigm to explore neural processes underlying visual-spatial WM (Funahashi, 2006; Scherf et al., 2006). In a classical ODR task an individual is shown a target location to remember during a short delay interval, generally in the range of seconds. At the end of the delay, the participant is required to make a saccade (eye movement) towards the target location (Srimal & Curtis, 2008). Correct task performance depends on the active maintenance of information and memory update, as the target stimulus location varies trial by trial. Thus, to attain an accurate response, the individual must use visual-spatial WM (Funahashi, 2006).

Expected patterns of connectivity vary based on the structural networks required for task-related behaviour (Fuster,1990; Fuster & Bressler, 2012). The neural evidence for WM is the

persistent neural activity observed between a sensory cue and a contingent future motor act (Curtis et al., 2004; Fuster & Alexander, 1971; Goldman-Rakic, 1989; Srimal & Curtis, 2008). In the ODR task this persistent neural activity is elicited in frontal and parietal cortical areas (Funahashi, 2006). Although there is evidence of a frontal-parietal connectivity during the delay period, to this date research results with respect to the functional nature of the neural substrates underlying this network supporting visual-spatial WM remains equivocal.

For example in ODR tasks, the frontal eye fields (FEFs) appear to be more active during delays that require matching of a cue location whereas delays that do not require memory retention demonstrate more activity in the posterior parietal cortex and inferior frontal cortex (Curtis et al., 2004). Interestingly, memory performance has been predicted by delay-period activity of the frontal eye fields and memory-guided saccade accuracy has been correlated with the magnitude of this neural activity (Curtis et al., 2004; Offen et al., 2010; Scherf et al., 2006). Lee and Ahn (2013) speculate that FEFs have limited attentional resources, and thus, can maintain only a limited number of targets in memory. For this reason, the correlation between increased magnitude and accuracy in ODR tasks may indicate the memory storage capacity of the FEFs.

Event-Related Potentials and Slow Waves

The memory maintenance required in the delay period of ODR tasks makes it a significant time period to explore the activation of structures involved in the memory retention of visual-spatial information. The precise timing of delay period activity warrants a research methodology with high temporal resolution. For this reason, ERP is a complementary methodology to explore the timing and pattern of neural activations.

The ODR task paradigm and the temporal preciseness of EEG lend themselves well to investigations of neural mechanisms underlying cognitive function. As previously mentioned, ERPs reflect the activity of a large population of neurons that fire at the same time (Light et al., 2010). The mapping of neuronal activations allow for inference of when and where regions activate in the generation of a neural function. A consistent and replicable activation of regions at specific latencies infer that regional activations are supported by a network function (Luck, 2005). In ODR tasks the activation of frontal and parietal regions are known to be involved in functional neural network connectivity. However, it is the function of each region involved in the generation of a memory-based saccade that remains equivocal (Constantinidis & Wang, 2004). EEG and ERP provide a robust method to better understand the patterned activation of neural function that supports visual-spatial working memory.

ERPs are used across a breadth of research and can be analyzed with various statistical procedures (Luck, 2005). A constant of the ERP methodology is its representation of peak amplitude and wave frequency activity that follow a neural response elicited by a selected paradigm. The sustained and peak activity may be measured with components or wavelet analyses. Component based analysis requires the averaging of continuous data recorded during a specific time period of a single trial. Wavelet analyses examine the frequency band of a particular type of activity under examination.

An interesting feature of slow wave activity (5 – 8 Hz) is its overall rate of higher amplitude in comparison to peaks with shorter duration (Roberts et al., 2013). Higher amplitudes are thought to indicate a more synchronous and stable neural activity. More specifically it is thought that slow waves (low frequency) synchronize the firing of large populations of neurons, while higher frequencies synchronize the firing of small groups of neurons (Light et al., 2010). In

an EEG study, Monfort and Pouthas (2003) reported that frontal sites demonstrated increased amplitude of slow waves when working memory demands increased. These results indicated that frontal regions co-ordinate to retain information in working memory. However, the underlying neural activity that generates the slow wave and coordinates neuronal firing remains equivocal. The current study, therefore, used ODRs to explore the neural processes involved in brief retention of visual-spatial information.

Delay Period Activity

Of particular interest is the sustained slow-wave activity observed in the absence of stimuli during delay period phases of the ODR tasks. A localized sustainment of neural activity in frontal brain regions suggests a top-down approach of cognitive function. Vecera and Rizzo (2003) state that top-down processes engage cognitive functions and evoke active interpretation of a cue and response accordingly. In regard to visual-spatial short term memory networks, top down processes are a primary area of interest. Top down processes occur between the encoding and retrieval phases of DR/ODR tasks. The persistent activity observed between the two phases has been interpreted as an active retention of task relevant information in preparation for a response (Fuster & Alexander, 1971; Serences, Ester, Vogel, & Awh, 2009).

Early phases of ODR tasks require information processing in primary sensory areas, and retention and action planning in frontal regions. Funahasi et al. (1989) reported that the neurons located in prefrontal areas have memory fields. Funahashi et al. defined memory field activity as the maximal firing of a neuron to the representation of a target in the visual field. Most importantly, Tsujimoto and Postle (2011) demonstrated that the magnitude of this sustained activity differs with the location of a cued target. This characteristic is key in recognition of the neural correlates underlying visual-spatial WM. It has been suggested that neural activity during

a delay period may be related to the cortical preparation of a saccadic response (Constantinidis & Wang, 2004). A cognitive process underlying preparation of an oculomotor response includes retention of visual-spatial information. However, the precise function of regions that support visual-spatial WM remains ambiguous.

During the delay period of ODR tasks, Bruce and Goldberg (1985) observed an activation of the frontal eye fields (FEF) in electrophysiological investigations of memory-guided saccades with monkeys. FEF is thought to be a neural substrate that has a unique contribution to memory-guided saccadic movement (Hutton, 2008). FEF is the major cortical eye field involved in saccade production and control, and is located in the anterior bank of the arcuate sulcus (Bruce & Goldberg, 1985). In humans, the EEG activity in the FEF during delay period phases of ODR tasks may reflect memory maintenance of the information required for an accurate behavioural response (Srimal & Curtis, 2008). Research has speculated that motor coding may be represented in the sustained neural activity observed at frontal eye fields (FEFs) in ODRs (Curtis et al., 2004; Offen, Gardner, Schluppeck & Heeger, 2010; Postle, 2006).

Frontal lobe oculomotor regions (i.e., FEF) appear to be more active in ODR delays that require matching of a cue location; ODR delays that do not require memory retention demonstrate more activity in the posterior parietal cortex and inferior frontal cortex (Curtis, 2004). Interestingly, memory-dependent tasks have been predicted by delay-period activity of the FEF and memory-guided saccade accuracy has been correlated with magnitude of neural activity (Curtis et al., 2004; Offen et al., 2010; Scherf et al., 2006). In ODR tasks a particular focus of interest has been on the persistent neural activity observed over the frontal and parietal areas during the delay period (Fuster& Alexander, 1971; Srimal&Curtis, 2008).

Frontal-Parietal Functional Units Underlying Visual-Spatial WM

Evolving from Fuster's (1973) early investigations of the prefrontal cortex, recent research has demonstrated neural network activity that persists within cortical regions when visual-spatial WM is engaged (Constantinidis & Wang, 2004; Singh, Kim, & Singh, 2003). The understanding that functions of WM are dependent on a series of neural networks in the brain is a fairly recent advancement in the field (Constantinidis & Wang, 2004; Johnson & de Haan, 2011; Singh et al., 2003). More specifically, a pattern of neural activity associated with visual-spatial WM has been observed in the fronto–parietal regions (Constantinidis & Wang, 2004; Srimal & Curtis, 2008). Parietal areas include the posterior parietal cortex and intraparietal sulcus for sensory processing and spatial transformation respectively (Constantinidis & Wang, 2004).

The general function of the parietal lobe is to integrate sensory information from various modalities (Constantinidis & Wang, 2004). In direct significance to this study its function includes determination of spatial location and navigation. The posterior parietal areas are responsible for the integration of visual-spatial information (Postle, 2006). The more basic sensory processes, such as colour recognition and visual perception, occur within the occipital regions. In consideration of Fuster's physiological definition of WM as cross-temporal mediation, there is a notable distinction between isolated sensory functions and more advanced visual-spatial processes.

The dLPFC is a major frontal association area that is involved in the temporary maintenance of visual-spatial and motor information, stimulus features, and task rules (Funahashi, 2006; Voytek & Knight, 2010). Another frontal structure involved in the maintenance of visual-spatial information is the ventral lateral PFC. Zimmer (2008) compared

cortical activations during a visual-spatial task with varied trial difficulty. In response to the varied task demands, differential activations of the ventral lateral PFC and dLPFC were observed. Zimmer (2008) contends that the ventral lateral PFC may be involved during more passive tasks, whereas the dLPFC becomes engaged during more active and demanding tasks.

Along with primary sensory areas, perceptual mechanisms are involved in the processing of visual-spatial WM. According to Postle (2006) prospective and retrospective motor coding are perceptual mechanisms involved in the retention of spatial information. A prospective motor code transforms vision-based coordinates into a motor plan whereas a retrospective motor code integrates information from a past perceptual event. Postle (2006) contends that mechanisms of motor coding are engaged during delay period activity, and are a cognitive mechanism that is represented by distinct neuronal activity.

Saccade Generation, Saccade Control and Memory-Guided Saccades in ODR tasks

Researchers have been investigating the cascade of neuronal activity that precedes saccadic movements for decades (Bruce & Goldberg, 1985; Berman, Joiner, Cavanaugh &Wurtz, 2009; Segraves & Park, 1993). Research on monkeys has revealed that several cortical areas become activated in the generation of saccades (Bruce & Goldberg, 1985; Segraves & Park, 1993; Wardak, Ibos, Duhamel, & Olivier, 2006). Segraves and Park (1993) examined the association between the FEF and the superior colliculus in the saccade dynamics of monkeys. Results from Segraves and Park's study suggest that the FEF and the superior colliculus can generate saccades in the absence of one another. This finding is significant in revealing that FEF is the only cortical area capable of independent saccadic activation.

However, in a study that examined saccadic function in monkeys with an ablated superior colliculus, Hanes and Wurtz (2001) contend that FEF is unable to independently support

saccades. Moreover, Hanes and Wurtz (2001) suggest that any recovery of saccadic function following ablation is a result of neural plasticity, rather than FEF being an already functioning pathway. Along with Segraves and Park (1993) and Hanes and Wurtz (2001), researchers have examined the FEF, the supplementary eye field, the superior colliculus and the posterior parietal cortex in the exploration of saccadic generation and control (Bruce & Goldberg 1985; Schlag & Schlag-Rey, 1985; Boch & Goldberg 1989).

Given the extensive research, it is suggested that anatomical and network related activations of visual-spatial WM memory may recruit specific functions of the FEF (Hutton, 2008). Research has suggested that activity in the dLPFC may be representative of saccadic planning in visual-spatial WM (Zimmer, 2008). Saccadic planning involves the maintenance of oculomotor coordinates for eye movements in response to specific task demands. Curtis et al. (2004) used fMRI to isolate the activation of anatomical regions by contrasting two spatial WM tasks. One of the tasks was a matching condition, in which eye movements could be planned and maintained during a delay period. The second task was a non-matching task in which planning could only occur at the end of the interval. Correspondingly, higher activity was observed in the FEF of the matching condition in contrast to the non-matching condition.

Interestingly, the non-matching condition showed higher activity within the intraparietal sulcus. Curtis et al. (2004) suggest that the observed differences may be related to task specific demands. For example, in the non-matching condition participants had to rely more on sensory information, which would explain the increased activity observed in the intraparietal sulcus. A study by Offen et al. (2010) observed an increase in activation at the FEF with task-related saccadic preparation supporting Curtis et al.'s (2004) findings. Moreover, Offen et al. (2010)

reported specific FEF activation patterns during a sustained delay period in WM and attention based tasks.

Saccade Generation, Saccade Control and Memory-Guided Saccades in EEG

Electrophysiological studies with non-human primates have measured the latency between the presentation of a stimulus and the preparation of a saccadic response (Carpenter, 1981; Hutton, 2008; Sparks & Mays, 1990). These studies have demonstrated that it takes approximately 40 ms for a signal to be transmitted from the retina to the superior colliculus, and an additional 20 ms for stimulation of the superior colliculus to generate a saccadic eye movement to a specific location (Carpenter, 1981; Sparks & Mays, 1990). Interestingly, the average latency of a human saccadic response is approximately 200 ms (Hutton, 2008). Hutton (2008) suggests that the delay in saccade response may be the result of a multitude of factors, including a period of decision processing that requires the recruitment of cognitive control structures. For this reason, Hutton (2008) contends that cognitive resources are used in the control of saccadic behaviour. Additionally, Bruce and Goldberg (1985) suggest that FEF may also be involved in the generation of memory-guided saccades.

Literature examining the neural substrates of memory-guided saccades in humans has demonstrated patterns in the behavioural component of saccadic activity (Hutton, 2008; Scherf et al. 2006). Scherf et al. (2006) describe the series of processes involved in visual responses to target stimuli. The authors explain that the first saccade is made to approximate a target location. This initial movement is triggered by processes that support voluntary responses, such as directing eye gaze to a location with no visual guidance. Scherf et al. (2006) further suggest that short-term memory processes become engaged in order to maintain an active representation of the target location. Following the initial eye gaze, subsequent corrective micro-saccades are

observed towards the remembered location. Luna et al.(2008) suggest that the observed corrective micro-saccades are representative of the target location held in WM and processes of error/performance monitoring. As outlined in the research (Curtis et al., 2004; Offen et al., 2010; Postle, 2006; Zimmer, 2008) the ability to control saccadic movements is an integral component of the visual-spatial information processing network.

In sum, evolving from Fuster's (1973) early investigations of the prefrontal cortex, research has demonstrated the activation of integrative cortical networks in visual-spatial WM (Constantinidis& Wang, 2004; Singh et al., 2003). More specifically, a pattern of neural activity has been observed at the fronto–parietal functional regions (Constantinidis& Wang, 2004; Srimal& Curtis,2008). The basic processing stream involves the initial detection of sensory input at the posterior parietal cortex, an area of the dorsal visual stream (Constantinidis & Wang, 2004). The sensory input may undergo spatial transformations or manipulation in the intraparietal sulcus, which is located within the parietal cortex (Brignani, Bortelleto, Miniussi, & Maioli, 2010). From the parietal cortex the sensory input is streamed to the dorsolateral prefrontal cortex (Funahashi, 2006). The frontal areas become engaged for the temporary maintenance of visual-spatial information, motor information, stimulus features, or task rules (Funahashi, 2006; Voytek & Knight, 2010). The consistent and replicable activation of parietal and frontal regions in visual-spatial WM, (Brigani, Lepsien, Rushworth & Nobre, 2009; Brigani et al., 2010; Postle, 2006), have supported further investigation of the neural networks underlying its function.

Saccade Generation, Saccade Control and Memory-Guided Saccades in Localization

As outlined in the research (Curtis & Srimal, 2004; Postle, 2006; Zimmer, 2008) the precise physiological processes and associated cognitive functions of the visual-spatial WM

network remains equivocal. To better understand the processes underlying the visual-spatial network, EEG studies have begun to incorporate methods of source localization (Grech, Cassar, Muscat, Camilleri, Fabri, Zervakis, Xanthopoulos, Sakkalis, & Vanrumste, 2008; Hönegger, Attenedera, Griesmayra, Holza, Webera, & Sauseng, 2011). Source localization is a solution to the inverse problem associated with EEG methodology (Grech et al., 2008). The inverse problem is a methodological issue in determining the anatomical source associated with EEG waves. In conjunction with the inverse problem, EEG data is contaminated by errors of source-modelling and noise, and thus creates a confound in determining accuracy of localized activity. However, by using models for neural activity and dipole fits, source localization can allow for spatial and temporal accuracy of up to 5mm (Grech et al., 2008).

sLORETA is a method that supports explorations of source localization with EEG data. The data processing software can reliably source information because it eliminates biological noise and measurement errors. In order to eliminate these errors, sLORETA utilizes a standard head model that is created by averaging variations in head shape. This deterministic model uses dipoles for precise and consistent locations of EEG data (Grech et al., 2008). In solving this localization error, the inverse problem that confounds EEG research is controlled. sLORETA is an important tool as exploration of localized neural brain sources can reveal cortical organization and the integration of neural resources (Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002). SLORETA was used in this study to explore the neural substrates underlying visual-spatial working memory.

The manner in which sLORETA was used in this study is a limitation of the results. Further analyses are required to determine the statistical significance of the localized activity that was detected. It will be necessary to examine the final results with consideration of the

methodological limitations of sLORETA; most notably its claim of zero-error source localization. This claim attests that the maximal activation observed is the actual source of localized neural activity (Pascual-Marqui et al., 2002). The claim of zero-error source localization is met with some scepticism throughout the scientific community. However, source localization of EEG data provides a model to explore anatomical activations in network functions.

Developmental Influences on Visual-Spatial WM Function

Animal studies were the catalyst and provide much of the framework for neural investigations of visual-spatial WM (Funahashi., Bruce, & Goldman-Rakic, 1987; Fuster, 1985; Goldman-Rakic, 1987; Jacobsen, 1936). In monkeys the prefrontal region for spatial WM is located near the anterior of the frontal eye fields, which is on the anterior bank of the arcuate sulcus (Bruce & Goldberg, 1985). Given that visual-spatial WM regions are within that area in monkeys (Funahashi et al., 1989), functional brain imaging studies of spatial working memory in humans also focus on the dorsolateral frontal region. Research using ODR tasks as a measure of visual-spatial WM function have consistently reported active memory retention in frontal regions of the DLPFC (Curtis et al., 2004; Luna et al., 2010; Srimal & Curtis, 2008; Zollig et al., 2010). The DLPFC is known to support a short-term retention of precise locations in space (Curtis, Rao, & D'Esposito, 2004).

Given the breadth of research on the neural substrates that underlie visual-spatial WM function (Fuster & Alexander, 1971; Fuster & Bressler, 2012; Srimal & Curtis, 2008), recent research has begun to explore how development influences these processes (Luna et al., 2010; Srimal & Curtis, 2008; Zollig et al., 2010). To examine the developmental trajectory of visual-

spatial WM networks, it is necessary to examine cortical responses related to visual-spatial WM function and explore variations between age groups.

It is well known that WM is a cognitive function that develops and adapts across the life span (Kemps, Rammelaere, & Desmet, 2000). In investigations utilizing Baddley and Hitch's (1974) model, development has been shown to influence the processing of phonological and visual-spatial information, and the attentional control resources of the central executive (Kemps et al., 2000; Postle, 2006). The developmental changes that occur in WM are closely associated with maturation of central executive functions (Baddeley, 2003). Functions of the central executive include, for example, response inhibition, attentional control and logical thinking, which are supported by frontal brain regions, as substantiated in neuro-imaging studies (Cornoldi & Vecchi, 2003; Hönegger et al., 2011; Smith et al., 1998; Thomason et al., 2009; Wager & Smith, 2003; Zollig et al., 2010).

The notable change in the structural maturation of the frontal lobe (Asato, Terwiilliger, Woo, & Luna, 2010), and its related cognitive functions are an interesting area of focus. However, more investigations are needed to better understand the implications of development on WM network function and efficiency. For example, the frontal-parietal structures recruited have been shown to differ across age groups, most significantly in the efficiency of network activation measured by latency-related differences (Zollig et al., 2010). In an ERP study, Zollig et al. (2010) utilize a prospective memory paradigm to explore differences in neurally generated compensational strategies. The authors operationally define compensation as a process that enables successful task performance (i.e., accurate responses despite a reduced function of brain regions that normally mediate response). Source localization with standardized low-resolution electromagnetic tomography (sLORETA) demonstrated compensational activations in

adolescents (11–13 years) and young adults (18–25 years) when compared to older adults (64–79 years).

More specifically, a higher activation of secondary occipital regions (posterior) was observed in adolescents at 500–1200 ms with a maximum of approximately 800 msec. In contrast, older adults maintained greater activation of prefrontal regions (anterior) at 700 ms, persisting until 1200 ms and expanding to middle temporal regions. Zollig et al. (2010) suggest that adolescents and older adults recruit more neural generators than young adults to attain response accuracy. The compensational mechanism may be due to the relatively late maturation of prefrontal regions in adolescents. Zollig et al. (2010) further suggest that the adolescent brain compensates for the reduced input from the prefrontal regions by relying more on sensory structures.

Research has suggested the circuitry underlying visual-spatial WM is established during childhood and becomes more refined and specialized throughout adolescence (Geier, Garver, Terwilliger & Luna, 2009). Functional differences that align with the maturation of the cerebral cortex include increased efficiency in the recruitment of anatomical structures (Geier et al., 2009; Zollig et al.,2010). Zollig et al. (2010) use ERP and sLORETA analyses to explore the neural circuitry of visual-spatial WM across age groups. In corroboration of the existing literature (Fuster & Alexander, 1971; Srimal & Curtis, 2008), the pattern of regional activations did not vary with age; however, differences were observed in the amplitude and sustainment of neural activity in specific regions. The transmission related time differences observed in Zollig et al's (2010) study are attributed to the high temporal resolution of EEG. Similar to Zollig et al.'s (2010) research conclusions, Asato et al.(2010) report that adolescents exert more effort and/or are less efficient in their ability to recruit brain regions, which may reflect underlying structural

immaturities. So while adolescents recruit similar regions as adults in tasks requiring visual-spatial WM, several maturational processes and age related differences are associated with its precise function (Klingberg, 2006; Olesen, Nagy, Westerberg & Klingberg, 2003).

Maturational processes in the visual-spatial WM network are of particular interest given that the frontal cortex is among the last brain regions to myelinate (Glasser & Easten, 2011). The relatively late myelination of the frontal cortex is similar to the inferior parietal cortex, and temporal cortex, which suggests an association among the regions (Glasser & Easten, 2011). The process of myelination is presumed to enhance transmission speed within the parietal cortex, as well as between the fontal and parietal cortices (Klingberg, Forssberg & Westerberg, 2002). More specifically, Klingberg et al. (2002) suggest that age related changes in myelination may increase cortico-cortical excitation and metabolism in the fronto-parietal network. Myelination constitutes white brain matter, and an increase in white matter volume supports the connections that may aide in network functional efficiency (Klingberg, 2006; Olesen et al., 2003).

The coinciding structural and functional changes suggest that circuitry underlying visual-spatial WM adapts into a more efficient network (Scherf et al., 2006). The late myelination that occurs in the frontal cortex makes this a region of developmental significance (Klingberg, 2006; Olesen et al., 2003). Given the mediation between frontal and parietal structures (Klingberg, 2006), age related differences in visual-spatial WM function can be used to explore the physiology of brain maturation across the life-span (Scherf et al., 2006).

The Present Study

The present study explored the physiological and cortical substrates that subserve visual-spatial WM in adolescents and young adults. Given the known activation of the frontal-parietal network in visual-spatial WM, Fuster's (1985) definition of WM is complementary to

investigation of the cross-temporal mediation. Further, cross-temporal mediation is reliant upon slow waves to coordinate network processes. The neural processes that support visual-spatial WM are equivocal (Constantinidis & Wang, 2004), and slow wave activity remains under-investigated in EEG research (Monfort & Pouthas, 2003). ODR paradigms provide a model to explore the unique properties of visual-spatial WM (Funahashi, 2006), and investigate the function of slow waves in the retention of task-relevant information during delay phases (Monfort & Pouthas, 2003).

Research has used DR tasks to examine the fundamental physiology underlying the frontal-parietal network since the early 1920's (Fuster, 1973; Hutton, 2008; Jacobsen, 1936; Goldman-Rakic, 1987). Recently, research has begun to explore the developmental trajectory of frontal-parietal network processes that subserve visual-spatial WM function (Luna et al., 2010; Srimal & Clayton, 2007; Zollig et al., 2010). Maturation of the network is particularly interesting because of the late myelination in the frontal cortex (Glasser & Easten, 2011) and its cross-temporal mediation with parietal areas (Fuster, 1985).

In order to better understand how development influences these processes it is integral to examine neural processes related to visual-spatial WM function and explore variations between age-groups. In a recent ERP study with healthy young adults (N = 22) aged 18 to 33 (M = 21.9), Tekok-Kilic et al. (2011), reported task- related slow wave differences over frontal and parietal sites during the delay period of three ODR tasks. Specifically, a negative slow wave was observed during the early phase of the delay period over central scalp sites in Match and Non-Match conditions relative to the Control condition. This result was interpreted as an active maintenance of visual spatial information at Pz during the early phase of the delay period. During the late phase of the delay period, the Match condition produced a larger positive slow

wave over frontal sites compared to both Non-Match and Control conditions. This result was contextualized as neural activity that may be indicative of oculomotor planning at frontal sites. The results of Tekok-Kilic et al's (2011) study lend support for the involvement of frontal-parietal networks in motor-planning functions associated with visual-spatial WM during the delay periods of ODR tasks.

The current study compared task-related slow wave activity in young adults (18-34 years) and adolescents (14-17 years) during the delay period of three ODRs. The goal of this electrophysiology study was to use the well-defined oculomotor system to explore patterns of frontal-parietal visual-spatial WM networks in young adults and adolescents. In conjunction with slow wave data analysis, the research utilized sLORETA to explore cortical activations in an ODR task. Specifically our research questions were,

(1) Are there any differences in the slow wave scalp topography between young adults and adolescents during the early and late delay period of three ODR tasks with varying task demands?

(2) Are there differential activations of the neural networks underlying visual-spatial WM between young adults and adolescents during the delay period?

CHAPTER III

Methods

Participants

Fifteen healthy young adults aged 18 to 33 (M = 23.8), and 15 healthy adolescents aged 14-17 (M = 15.6) were recruited as part of an ongoing developmental ERP study (REB #10-211). Young adult participants were recruited through lab volunteers (first 10 participants for the pilot runs) and from undergraduate Brock students via course and poster announcements. Typically developing adolescents aged 14-17 were recruited from community volunteers via snowball sampling. Before acceptance into the study, participants were screened with verbal questionnaires to determine possible neurological (i.e., head trauma), psychiatric challenges (i.e., ADHD) and chronic health problems (i.e., Systemic Lupus) that can affect an EEG recording (Appendix C). All participants were native English speakers and reported normal or corrected to normal vision. Participants were provided a $20.00 honorarium for the two-hour testing session.

Data Acquisition and Processing

Three ODR tasks were developed with Eprime software (Version 2.0). EEG data were recorded using a 128-channel Netstation System, (Electrical Geodesics Inc.). Eye movement data were collected with Smart Eye Pro (Version 5.8). The processing of offline EEG data were conducted with Matlab (Mathworks, 2006), EEGLab (Version 12), and ERPScore (Segalowitz, 2011) softwares. Source localization images of the EEG data were processed with Low Resolution Brain Electromagnetic Tomography (sLORETA, 2008).

Oculomotor Delayed Response Tasks

General Task Parameters

Each of the three ODR tasks had 8 locations where a white-star stimulus appeared (Appendix E). All tasks had 64 trials that were delivered in two blocks, with a break at the midpoint. The total running time for each task was eight minutes. All tasks repeated the same sequence of 64 stimuli that appeared in 1 of 8 pre-defined screen locations. An initial 1500 millisecond fixation period was followed with a 200 millisecond cue phase at which point the stimulus presented on screen. After the presentation of cue and stimulus, a 2500 millisecond delay period occurred. At the end of the delay period, the fixation stimulus disappeared for a 1500 millisecond response phase. During the response phase participants were required to gaze in the direction of the remembered stimulus location. Participants were asked to withhold any blinks from the moment the cue was presented until end of saccade movement in response phase. After the response, a 1000 millisecond feedback phase presented a small spaceship at the accurate stimulus location. A 1000 millisecond inter-trial interval (ITI) occurred before the start of the next trial.

Match Condition

The Match condition required participants' to keep task-related instructions and the location of a stimulus in mind. During the delay period, participants were instructed to remember the position of the white star stimulus and maintain gaze upon a fixation. In the response phase the participants were required to make a saccade (memory-guided saccade) to the location where the stimulus was given during the cue period. In this condition, the participants were expected to use the information retained in memory to generate a saccadic response toward the remembered spatial location until feedback stimulus appeared.

Non-match Condition

The Non-match condition required memory retention of task specific instructions, stimulus location, and response inhibition. The stimuli appeared in one of eight spatial locations around the fixation. Participants were instructed to maintain fixation, and remember the spatial location of the cue throughout the delay period. During the response phase, two star stimuli were presented simultaneously, one in the initial location and a second in a new location. Participants were instructed to inhibit gaze towards the initial cue position and to make a saccade towards the new location. Feedback stimulus would indicate if the participant had accurately responded in the trial.

Control C*ondition*

The control condition was designed to provide a baseline measure of EEG data, saccadic movement, and cortical activation. The cue stimulus was overlaid on the fixation stimulus and participants were instructed to prepare for the generation of a saccade. During the response period, a star stimulus (identical to the cue stimulus) was presented in one of the eight spatial locations around fixation. Participants were required to make a saccade to the cued location and maintain gaze until feedback stimulus appeared.

Eye Tracking

Eye movements were monitored with Smart Eye Pro System (Version 5.8). The system has two infrared cameras mounted on the two sides of the 19 inch monitor used in the testing room. Camera calibrations were completed for each participant before each testing because of individual differences in facial features (i.e., eye contour etc). For this study eye tracking was used only to monitor eye movements. An accurate response was determined by measuring pixel location and matching the participants gaze fixation to correct stimulus location.

Electrophysiological Recording

Participants were tested in the Developmental Neuroscience Laboratory, located in the Department of Child and Youth Studies at Brock University. All recordings were completed in an electrically shielded sound-attenuated chamber. Continuous EEG was collected and stored with Netstation EEG Software, using a 128 channel Hydrocel Sensor Net (Electrical Geodesics Inc.); sampling rate was kept at 500 Hz. The data were filtered during acquisition with a bandpass of 0.1-100 Hz and vertex was used as reference. Channel impedances were kept below 100 kΩ.at all times.

Data Processing and Reduction

Data Transfer

After acquisition, the continuous data were exported from Netstation to MATLAB (MathWorks, 2006) for off line processing. Continuous EEG for each participant was transferred to EEGLab which operates within MATLAB.

Continuous Data

The continuous EEG was re-referenced to mastoid sites (E55 and E100). The EEG was tagged with the exact left and right cue positions for Match and Non-Match conditions. The data was filtered with a low pass filter to remove any frequencies above 30Hz.

Segmentation Procedures

The filtered data for each subject was segmented into 2900 millisecond epochs which included 200 millisecond prestimulus interval, 200 ms cue period and 2500 ms delay interval. 200 millisecond prestimulus interval was used for baseline correction. After segmentation, baseline was corrected to 0 for all 128 channels to control the signal to noise ratio. Baseline procedures use a systematic algorithm that takes the average of each channel in the data and

subtracts it from the overall average of the EEG data. The baseline of each channel should be relatively flat, with slight variations given the signal to noise ratio in the respective channel.

Artifact rejection

Eye Artifact Removal

Eye artifact removal was performed by using an eye regression algorithm that removes vertical blinks from the data. To conduct the eye regression, the EEG activity in extraorbital (channel 8) and the zygomatic (channel 126) were regressed out and re-added to the data via the addition of a new VEye channel.

Visual Editing for Artifact Rejection

Visual editing was conducted to detect artifacts that were not filtered out in the initial filtering such as minor body movements, sweating, and 60Hz electrical noise. The visual editing stage required a systematic approach to ensure consistency across all subjects. In the current study, the operational definition for artifact detection was activity that exceeded 60Hz (i.e., electrical noise) or trials that were not continuous with its nearest trial (i.e, due to participant or technical artifact). Based on these criteria, a decision was made to either interpolate a channel or remove the epoch. To ensure consistency, the channel was interpolated if significant noise was present across five or more epochs. No more than four channels were interpolated within subjects for the data that were included in final analyses. Alternatively, epochs were deleted if noise was not replicated across specific channels. In addition, detection of inaccurate responses was deleted from the data. A response was deemed inaccurate if saccadic movement and gaze fixation did not fall within the correct spatial location for each trial. During the visual editing stage, entire participant data was rejected if the number of rejected epochs in any condition exceeded twenty-five.

Averaging

The segmented and artifact rejected EEG was imported to ERPScore. In ERPScore the segmented EEG for each ODR was averaged for delay period activity. The Match and Non-match conditions were averaged for (1) Trials in which the stimuli presented at the left visual field (total 32 trials), (2) Trials in which the stimuli presented at the right visual field (32 trials) and (3) All trials-right and left visual fields collapsed (total 64 trials). For control condition the data was averaged only for all trials collapsed.

Defining ERP Components and Slow Wave Potentials

All ERP waveform analyses were performed in ERPScore software. Averaged waveforms were analyzed for delay period slow wave activity. In each ODR task, the delay period slow wave activity was defined as the sustained slow wave potential that started at approximately 600 millisecond post stimulus and lasted to the end of the delay period before initiation of a saccade. This latency is consistent with the previous reports from our lab (Tekok-Kilic et al, 2011). The amplitude of the slow wave was calculated as the average area of the waveform.

Source Localization

The final stage of data exploration was conducted using sLORETA. sLORETAwas used to convert ERP data into voxel space for source localization of regional activations in both groups in all three ODR conditions. sLORETA determined the regions that were a measure of best fit to represent where the neural activity was occurring within the brain (up to 5mm below the scalp). Visual representation of images was used to investigate expected activation of the frontal-parietal network in support of task demands requiring visual-spatial WM. In order to integrate EEG results, images were taken at the early (700 ms) and late windows (2700 ms) of delay period activity.

Procedure

Before Testing

Before coming to the lab all participants were screened to ensure medical conditions did not conflict with EEG testing. The screening process was conducted using a standard form that ensured that all data was collected from healthy and typically developing individuals. Consent forms were provided and signed by all participants, and their parents in cases where participants were under 18 years of age (Appendix A & B). Participants were briefed on the purpose of the study and the mechanics of the EEG and eye tracking equipment.

Circumference of the participant's head was measured to identify the appropriate net size. Accurate placement of the EEG net was conducted by measuring the midpoint from the inion to the glabella, and horizontally from one tragus to the other. A wax pencil was used to mark the intersecting location for placement of the vertex reference. The net was then fitted and adjusted to assure the accurate placement of 128-electrodes.

During Testing

During data acquisition, researchers monitored the EEG and eye tracking data via external monitors outside of the testing room. At the half way point of each task, a planned, open-ended break occurred and the researchers entered the testing room to check on the participant's comfort and/or re-calibrate equipment if necessary. Breaks also occurred between the three tasks during which the researcher checked on the participant and recommended that they take the opportunity to rest their eyes and stretch. During between-task breaks the impedance values were checked and adjusted when necessary. Testing itself took approximately 45 minutes with an additional 25 minutes in flex time available for breaks and to ensure equipment was functioning properly. At the conclusion of the testing session participants were provided with remuneration and provided

a debriefing form (Appendix D) that outlined the goal of the research study and contact information for lab personnel.

CHAPTER IV

Analyses and Results

Overview of the Analyses

This study involved a between group within subjects repeated design. The research variables were Group (Young Adult, Adolescent) x Condition (Match, Non-Match, Control) x Electrode site (Fz, Pz) x Window (700-1100 ms, 2200-2700 ms). An ANOVA with repeated measures was conducted with IBM SPSS Statistics (*version* 21) to compare early and late phases of delay period activity elicited by three ODR conditions at frontal and parietal sites in young adults and adolescents.

Outlier Analyses

A series of preliminary analyses were used to explore data in SPSS. The average slow wave amplitudes (i.e. area measures) in each ODR condition during early and late windows were screened for any individual outliers. Tukey's box plots were examined for outliers in two midline electrode sites (Fz, Pz) and time periods (700-1100ms, 2200-2700 ms) across all three conditions. One adolescent and one adult participant were detected as outliers in Match condition at Pz during time period 2200 to 2700 ms, and a second adolescent demonstrated extreme values across all conditions.

Population parameters and statistics supported the removal of data for one adult participant and two adolescent participants. Normality was assessed via superimposed normal probability curves on histograms of sample data. Skewness and kurtosis values were calculated to support the visual representation of normal distributions. Preliminary analyses conducted with outliers indicated that the Match condition had significant kurtosis (*z*kurtosis=2.03) at Pz and violated normality based on the Shapiro-Wilk test ($D = 0.69$, $p = 0.00$). The Control condition also

violated normality at Fz ($D = 0.90$, $p = 0.01$). Upon removal of participants with extreme amplitude values, Shapiro-Wilk tests concluded that all data from both groups were from a normal distribution ($p > 0.05$). The final data-set with outliers removed demonstrated a decreased standard deviation and decreased standard error of mean in all conditions at both electrode sites. Tables 3.1.and 3.2 show the means and the standard deviations of slow wave amplitudes across all conditions and electrode sites in young adults and adolescents respectively.

Table 3.1 Young Adults: Means (M) and Standard deviations (SD) of mean area values (average amplitudes in microvolts) for frontal midline (Fz) and parietal midline (Pz) scalp sites during early and late phases of delay period in three ODR tasks.

	Match				**Non-Match**				**Control**			
	Fz		Pz		Fz		Pz		Fz		Pz	
Window	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
700-1100	1.2	1.4	-0.4	1.7	0.8	2.1	-1.4	1.8	0.5	1.9	0.6	2.0
2200-2700	-4.1	4.3	-2.9	4.6	2.3	2.6	-2.9	6.9	1.9	1.7	1.6	3.3

Table 3.1. Young Adults: Means (M) and Standard deviations (SD) of mean area values (average amplitudes in uVs) for frontal central (Fz) and parietal central (Pz) scalp sites during early and late phases of delay period in three ODR tasks.

Table 3.2 Adolescents: Means (M) and Standard deviations (SD) of mean area values (average amplitudes in uVs) for frontal midline (Fz) and parietal midline (Pz) scalp sites during early and late phases of delay period in three ODR tasks.

	Match				**Non-Match**				**Control**			
	Fz		Pz		Fz		Pz		Fz		Pz	
Window	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
700-1100	0.3	2.0	0.4	1.7	0.3	2.1	0.5	3.3	1.3	1.6	0.3	3.1
2200-2700	0.4	3.0	-1.1	2.2	-1.4	2.1	-0.9	2.4	-0.2	2.2	0.1	4.5

Table 3.2 Adolescents: Means (M) and Standard deviations (SD) of mean area values (average amplitudes in uVs) for frontal central (Fz) and parietal central (Pz) scalp sites during early and late phases of delay period in three ODR tasks.

Main Analyses

ERP Area Measures

Area measures were calculated with ERPScore (Segalowitz, 2012) for all 128 electrode sites at eight different time windows (300-500 ms, 300-700 ms, 500-650 ms, 700-1100 ms, 800-1800 ms, 1000-1400 ms, 2000-2700 ms, 2200-2700 ms) during the 2500 ms delay period. The average amplitude values at Fz and Pz during 700-1100 ms and 2200-2700 ms were included in final analyses (N = 25). Figures 3.1 and 3.2 display the grand averages of SW potentials across all three conditions for young adults and adolescents. Figures 3.3, 3.4 and 3.5 display the ERP grand average waveforms for young adults and adolescents during the 2500 ms delay period in all three conditions. The relevant time windows are indicated with a rectangle at each waveform.

Figure 3.1. Grand averages of delay period SW potentials observed in three ODR conditions at Fz and Pz in young adults (black-control, red-match, blue-non match)

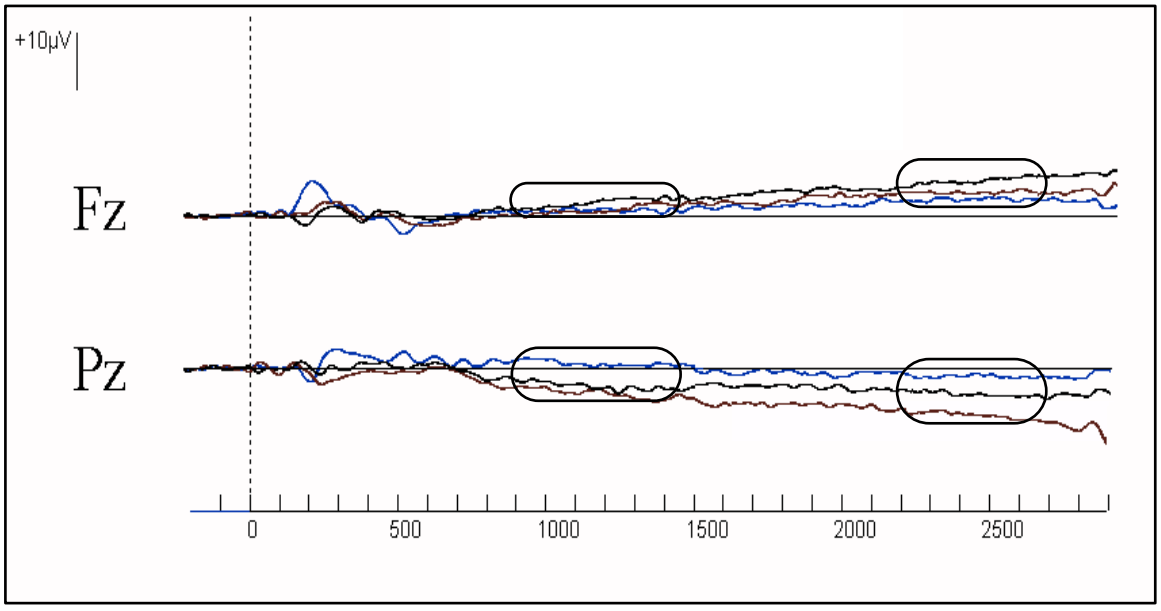


Figure 3.2.Grand averages of delay period SW potentials observed in three ODR conditions at Fz and Pz in adolescents (black-control, red-match, blue-non match) .

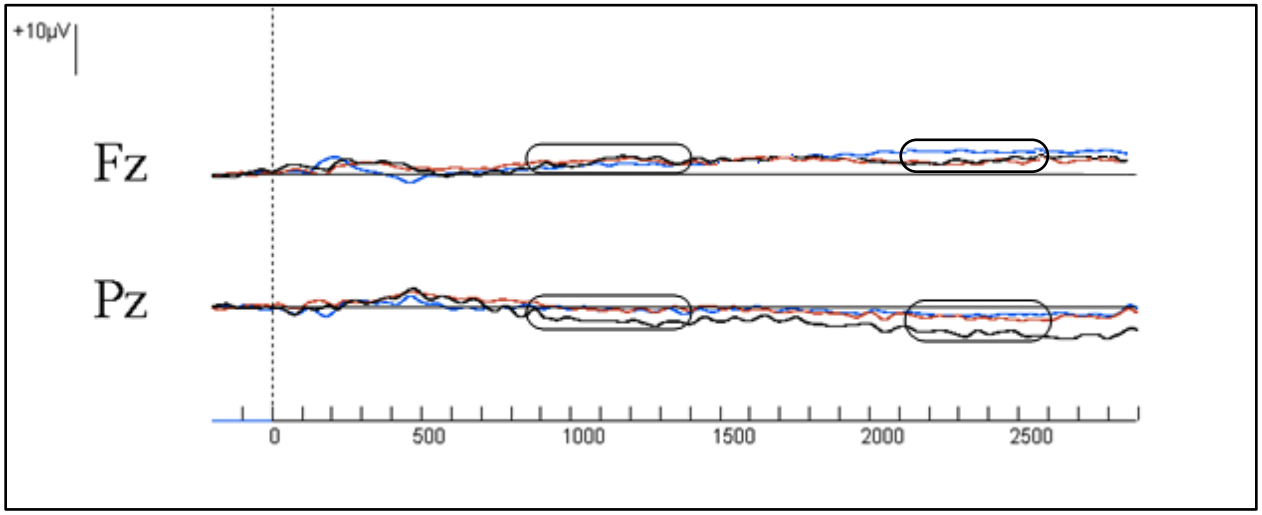


Figure 3.3.Control Condition- Grand averages of delay period SW potentials recorded at Fz and Pz (Blue-Adolescents, Red- Adults).

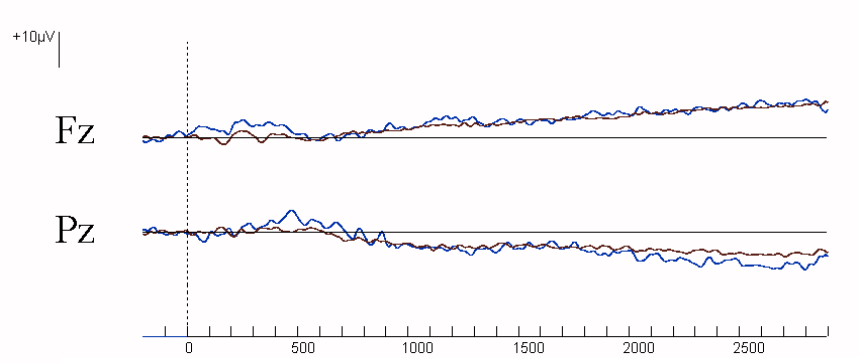


Figure 3.4.Match Condition- Grand averages of delay period SW potentials recorded at Fz and Pz (Blue-Adolescents, Red- Adults)

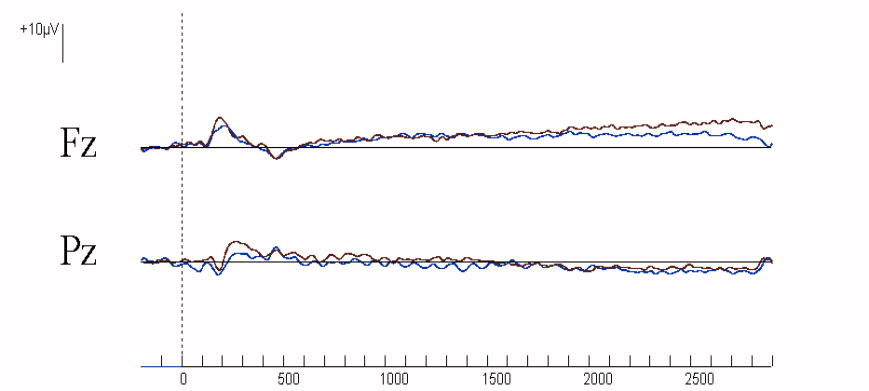
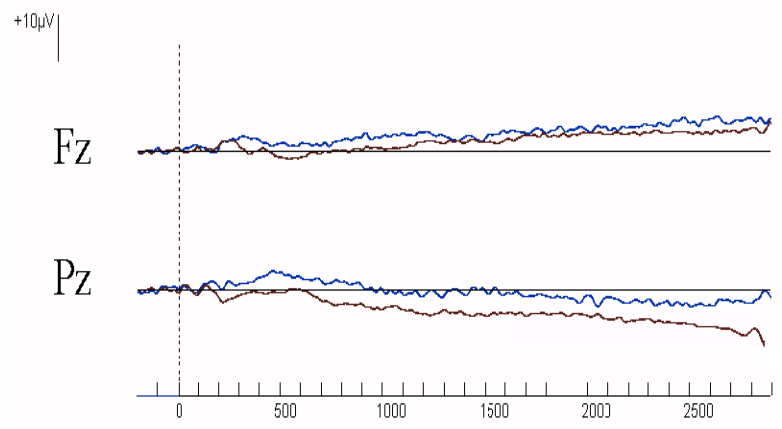


Figure 3.5.Non-Match Condition- Grand averages of delay period SW potentials recorded at Fz and Pz(Blue-Adolescents, Red- Adults)



Statistical Analyses

An ANOVA with Repeated Measures was conducted to explore the significant main and interactions effects of Group (Young Adult, Adolescent) x Condition (Match, Non-match, Control) x Electrode site (Fz and Pz) x Window (700-1100 ms, 2200-2700 ms). In all significant results greenhouse-geisser epsilon corrections were used.

The analysis revealed a significant electrode site main effect [F (1,46) =13.1, p=.001, partial η^2= .36], significant electrode site x group [F (1,46)=5.62., p=.026, partial η^2=.20], window x group [F (1,46)=6.86, p=.015, partial η^2= .23], window x electrode site [F(1,46)=6.93, p=.015, partial η^2= .23] two–way interactions and a significant condition x electrode site x window x group four way interaction [F (2, 46) = 3.21, p=0.05, partial η^2= .28]. This simple effect of the significant four-way interaction was analysed by Electrode site (2) x Window (2) x Group three-way ANOVA for the Match, Non-match and Control conditions separately.

Results of the Match Condition

The ANOVA results revealed significant Group [F (1,23)=6.48, p=.018, partial η^2= .34] and Electrode site [F (1, 24) =6.17, p=.021,partial η^2= .21] main effects, as well as significant electrode site x group [F (1,24)=4.33, p=.049, partial η^2= .16], window x group [F (1,24)=7.20, p=.013, partial η^2=.24], electrode site x window [F (1,24)=5.0, p=.035, partial η^2=.18] two-way interactions. Significant *electrode site x group* (Figure 3.6 & 3.7) and *window x group* interactions were further analyses for the simple effects (Figure 3.8).

Significant Electrode site x Group Interaction. This interaction was probed in two different ways. First, in order to investigate whether the overall slow wave amplitudes differed between age groups, the amplitudes across delay phases were collapsed and groups were compared in each electrode site in separate univariate analysis. The results revealed significant group

differences at Fz [$F(1,23)=7.96$; p=.010] but not at Pz [$F(1,23)=.17$; p=.68]. At Fz, regardless of the phase of the delay period (early versus late), the young adults had (M=2.61) significantly higher slow wave amplitudes compared to adolescents (M=-.068) (p=.01)

Figure 3.6. Match Condition: Frontal-Parietal scalp distribution of SW amplitudes during early phase of the delay period (700-1100 ms)

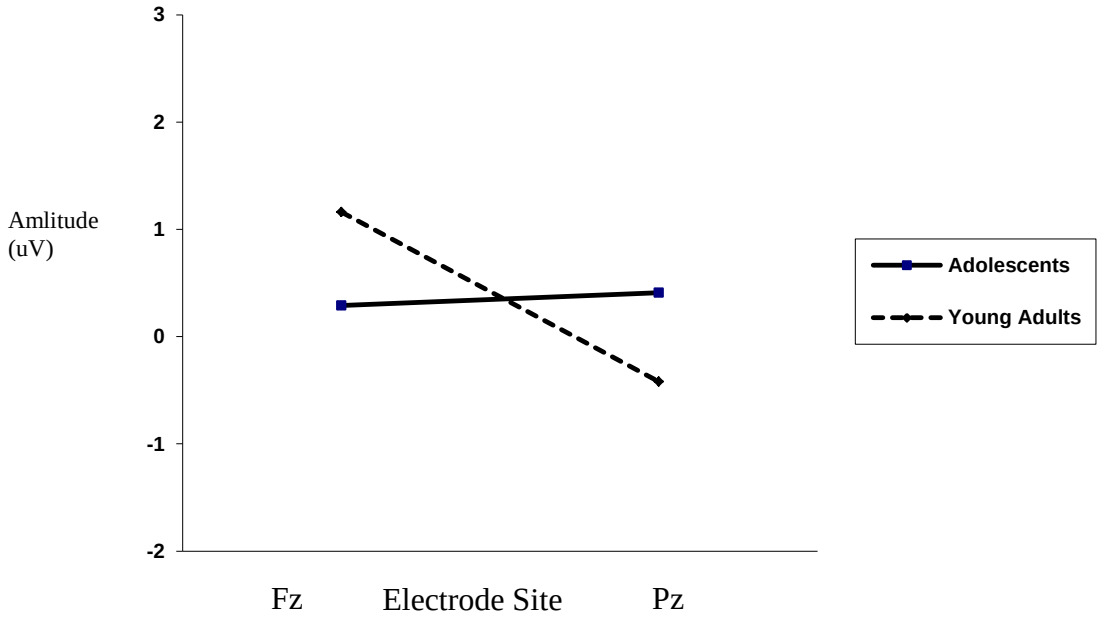
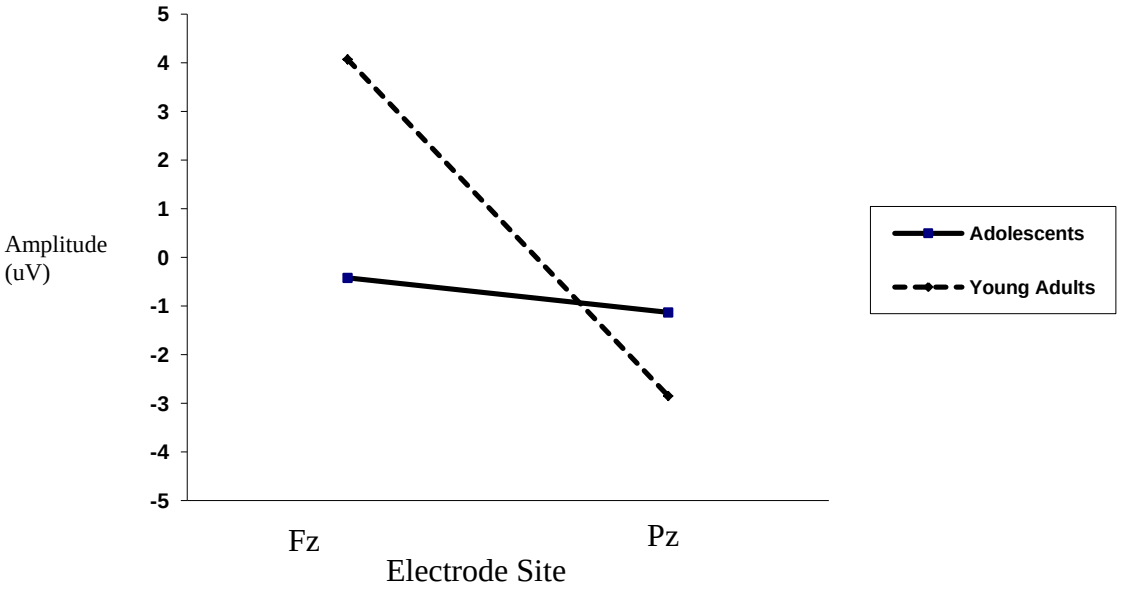
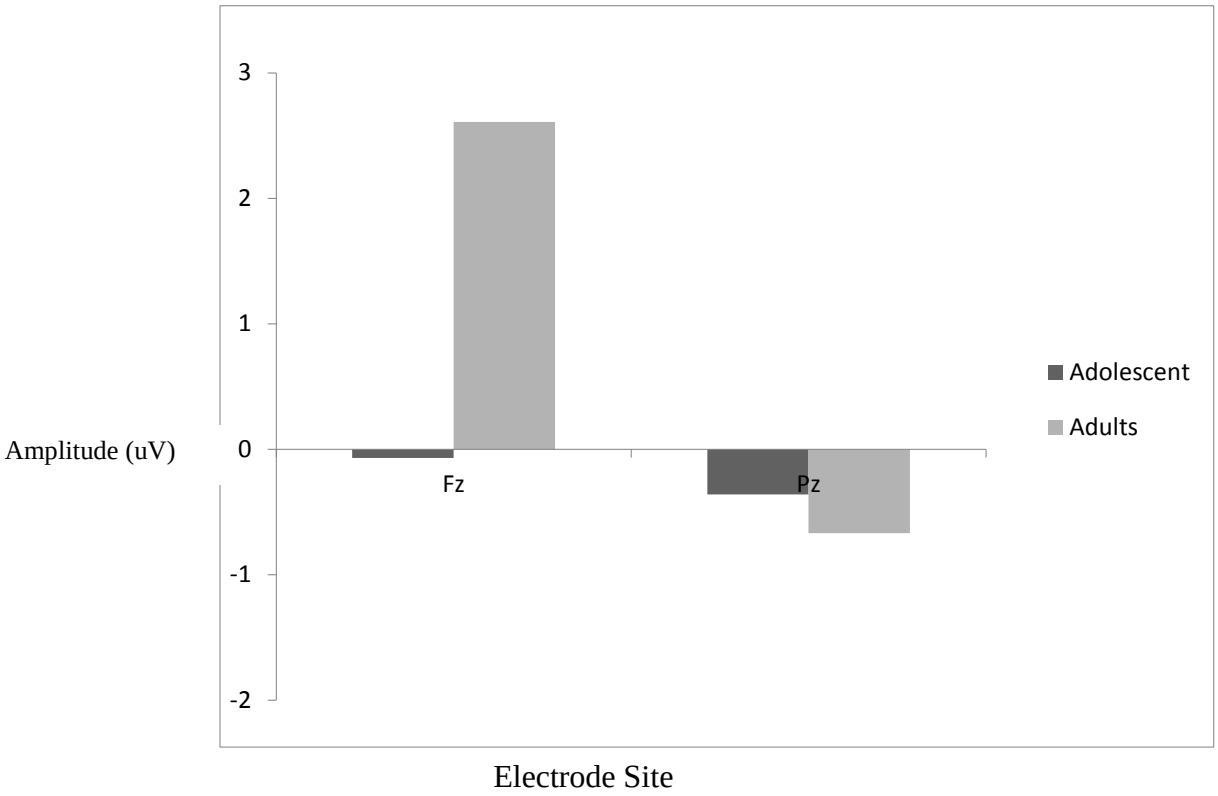


Figure 3.7. Match Condition: Frontal-Parietal scalp distribution of SW amplitudes during late phase of the delay period (2200-2700ms)



Second, in order to understand whether there is a scalp topographical difference (i.e. Fz versus Pz) within each age group, slow wave amplitudes at Fz and Pz electrode sites were compared for young adults and adolescents (Figure 3.8). The results showed that in young adults, regardless of the delay phase, slow wave amplitudes at Fz were significantly higher than amplitudes at Pz [$F(1,12)=10.84$, $p=0.06$, partial $\eta^2=.47$]. In adolescents Fz and Pz amplitudes did not show any significant difference [$F(1,12)=0.08$, $p=0.78$].

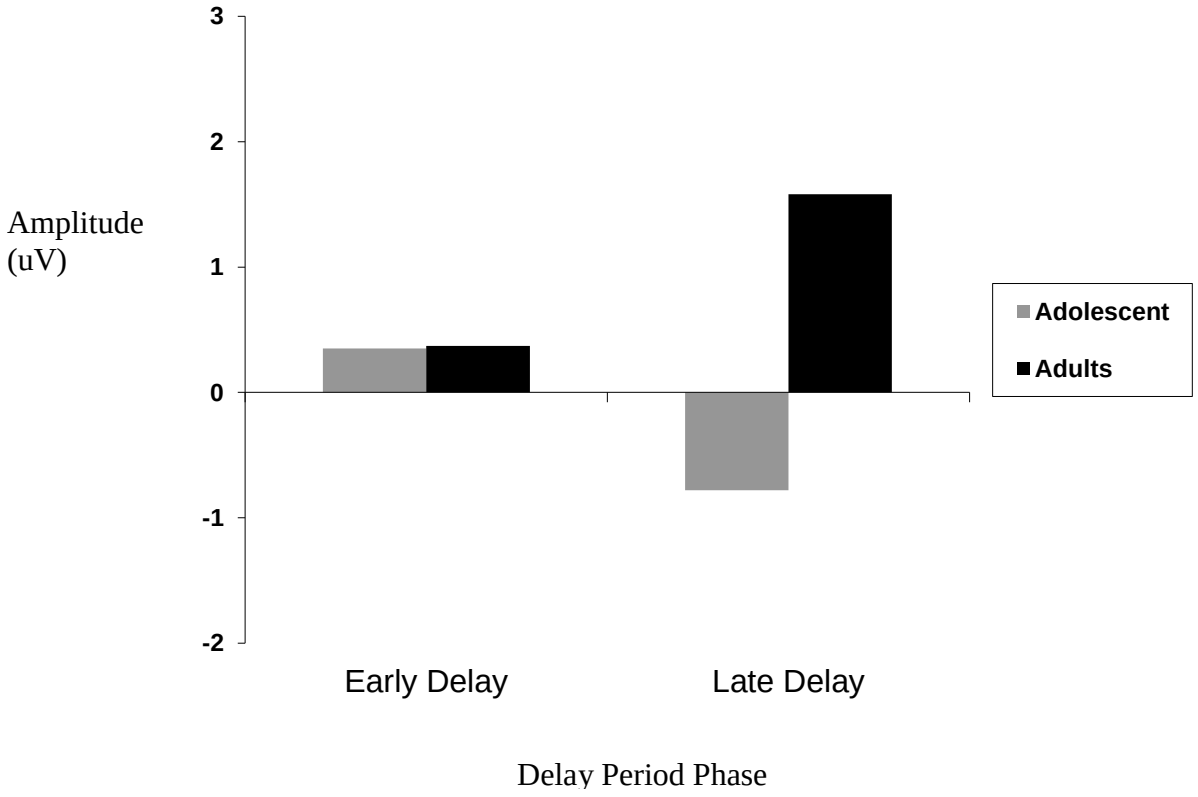
Figure 3.8.Significant differences in Frontal-Parietal scalp distribution of early and late SW amplitudes in Match Condition in young adults and adolescents.



In summary, during the Match condition, regardless of the phase of the delay period, the young adults had higher slow wave activity recoded at Fz compared to Pz. Adolescents, however, did not show significant differences in topographical distribution of slow waves between Fz and Pz.

Significant Window x Group Interaction (Figure 3.9). In order to investigate the simple effects, the slow wave amplitudes were collapsed across electrode sites and groups were compared in early and late delay period phases in separate analyses. Univariate results showed that during the early phase of the delay period, groups did not differ significantly [$F(1,23)=.001$, $p=.97$], but during the late delay period significant group differences were observed [$F(1,23)=9.19$, $p=.006$, partial $\eta^2=.28$]. In the late delay period, the young adults had higher slow wave amplitudes compared to adolescents.

Figure 3.9 Match condition: Window x Group Interaction.



Results of the Non-Match condition

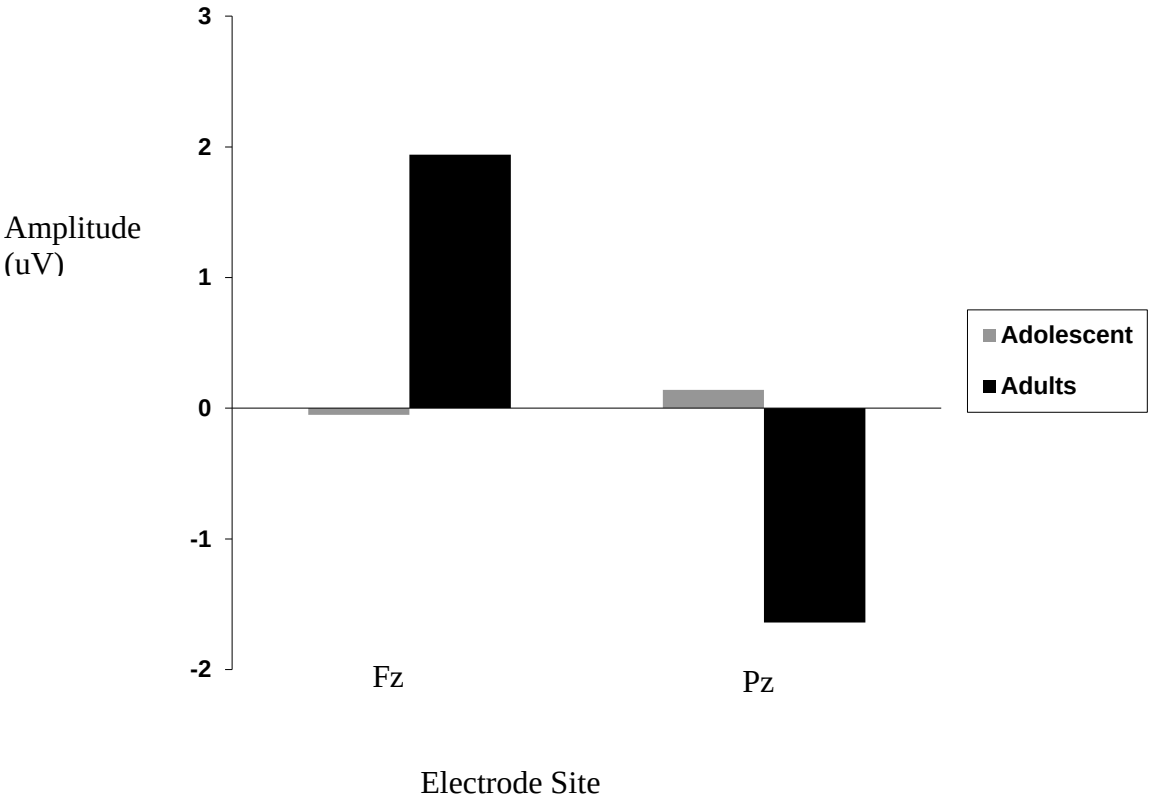
The ANOVA results revealed only a significant electrode site [*F* (1, 24) =10.59, p=.01,partial η^2= .32] main effect. There were no other significant two or three way interactions. Regardless of delay phase and age, slow wave amplitudes were significantly larger at Fz (M=1.11) compared to Pz (M=-0.68) (p=.003).

Results of the Control Condition

The Window (2) x Electrode Site (2) x Group (2) ANOVA results revealed a significant window x electrode site x group [*F* (1, 24) =8.07, p=.009, partial η^2=.26] three-way interaction. Other main and two-way interactions were not significant.

Three-way interaction was probed by two separate Electrode site x Group two-way mixed ANOVAs in each time window of the delay period. In the early delay period, there were no significant main or interaction effects. In the late delay period there was a significant electrode side main effect [*F* (1, 23)=5.22, p=.032] and a significant electrode site x group interaction [*F* (1,23)=6.20, p=.020]. Significant interaction in late delay period was analysed further in One-Way ANOVA comparing scalp distribution (i.e. Fz versus Pz) of the slow wave amplitudes between young adults and adolescents. The results of this analysis revealed a significant group difference at Fz [*F* (1,23)=6.23, p=.020] but not at Pz. Young adults had a larger and a positive slow wave (M=1.92) over Fz compared to adolescents (M=-.02). (Figure 3.10)

Figure 3.10 Control condition: Late delay period SW topographical differences between groups.



Visual Inspection of Possible Cortical Sources in Early and Late Delay Period

In order to explore possible cortical sources underlying scalp recorded SW activity during early and late phases of the delay periods, the ERP data was converted into voxel space for exploration of localized regional activations in sLORETA. Data from the entire 2500 ms delay period at all 128 electrode sites were included in the creation of images (see Figure 3.11, 3.12 & 3.13). Cortical activation at frontal and parietal sites was explored in the delay period activity of all three conditions. The significant electrode site effect in the Match condition for young adults at Fz was evident in the representation of voxel space data (see Figure 3.11). Although further statistical analyses are required to determine the significance of sLORETA results in this study, regions of interest along the fontal-parietal network did present with localized cortical activation.

The preliminary qualitative exploration indicated that the ODR paradigm used in this study engaged the frontal-parietal network to support visual-spatial WM. These results are demonstrated in the early and late windows of delay period ERP activity. Future analyses will test the significance of the correlations between voxel space data and pre-defined regions of interest that activate in visual-spatial WM function.

Figure 3.11.sLORETTAImages for the early and late delay phases of the Match condition. Rows depict the age groups, and columns depict the phase of the delay period.

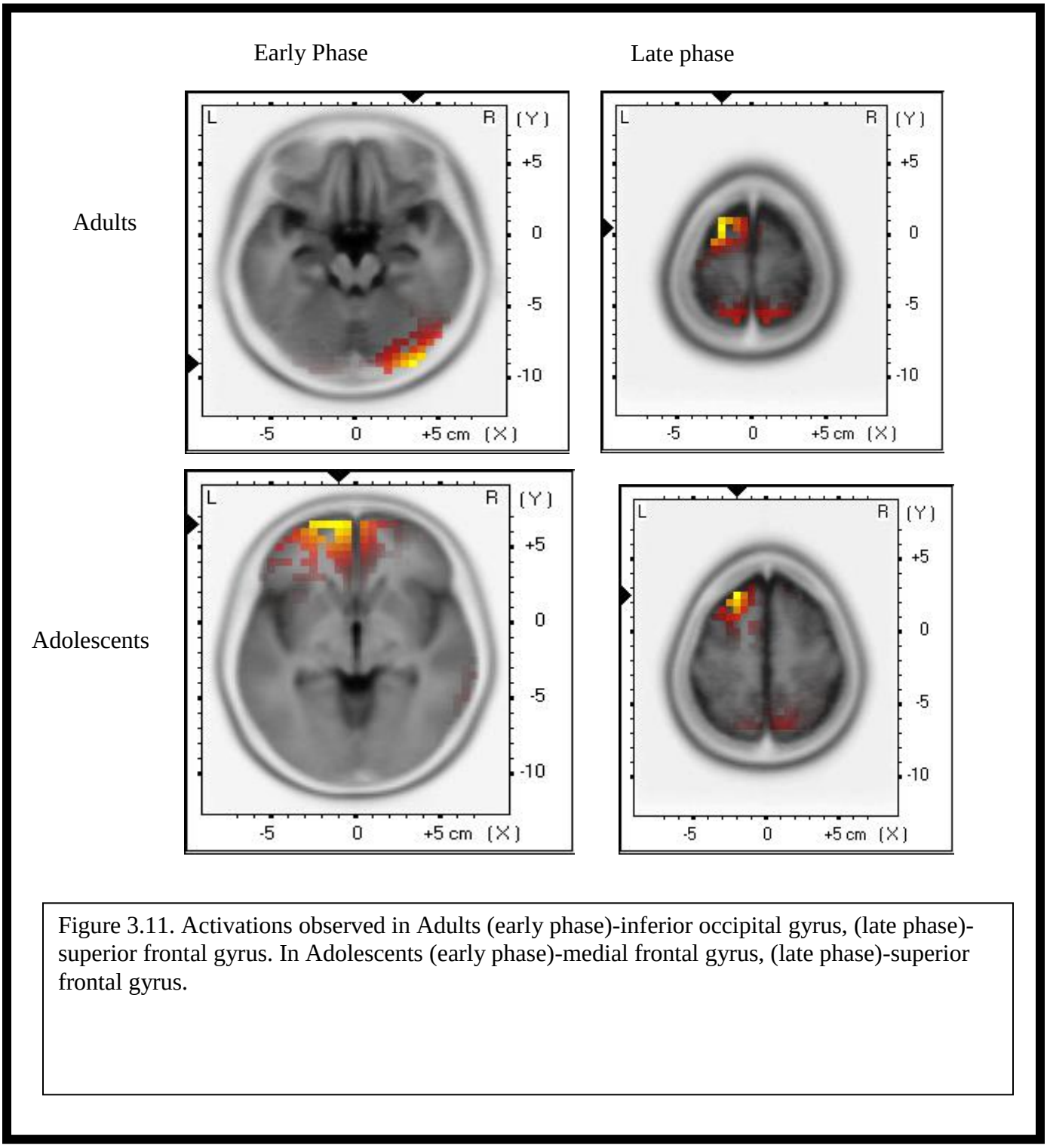


Figure 3.11. Activations observed in Adults (early phase)-inferior occipital gyrus, (late phase)-superior frontal gyrus. In Adolescents (early phase)-medial frontal gyrus, (late phase)-superior frontal gyrus.

3.12. sLORETTA Images for the early and late delay phases of the Non-match condition. Rows depict the age groups, and columns depict the phase of the delay period

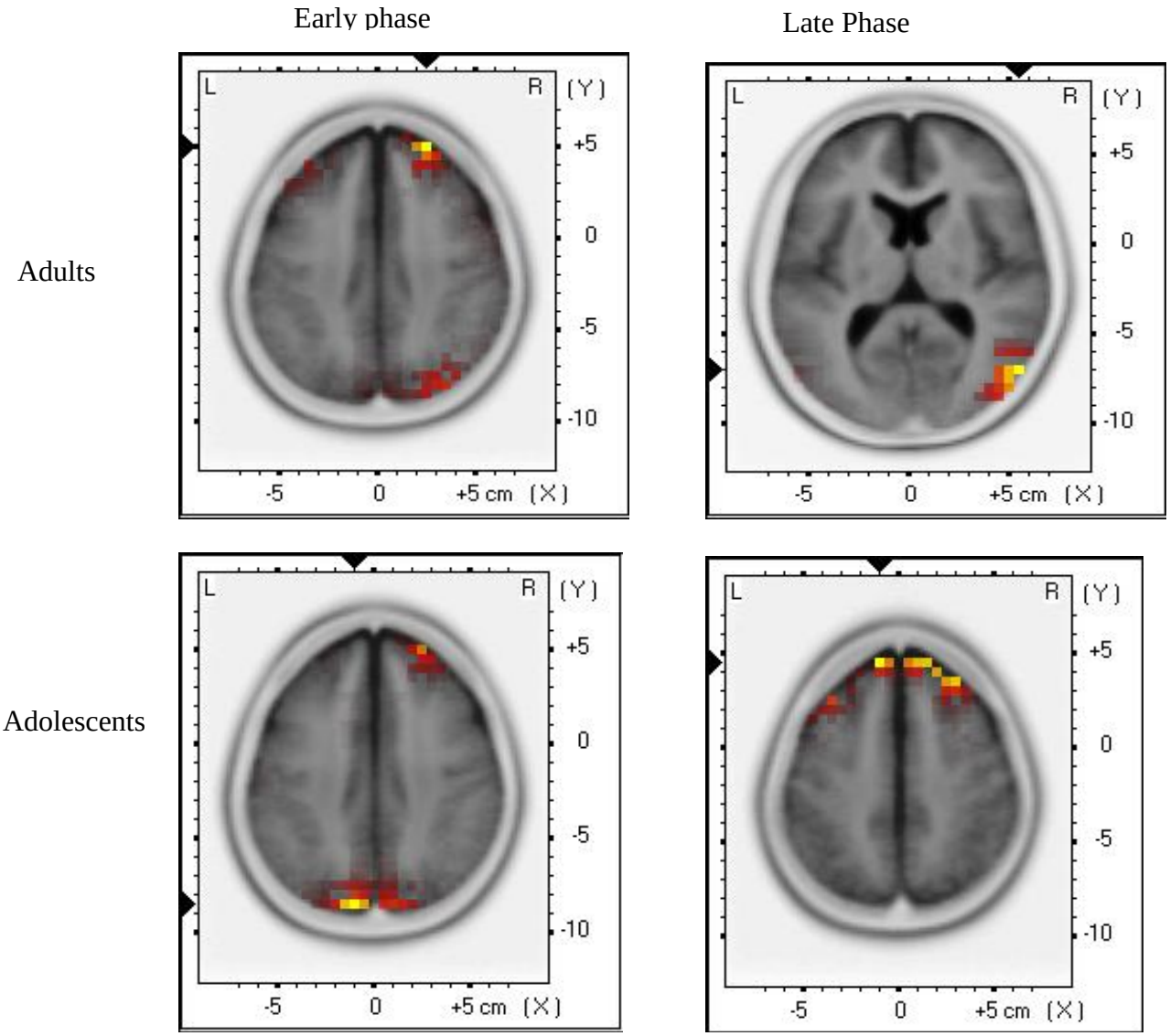


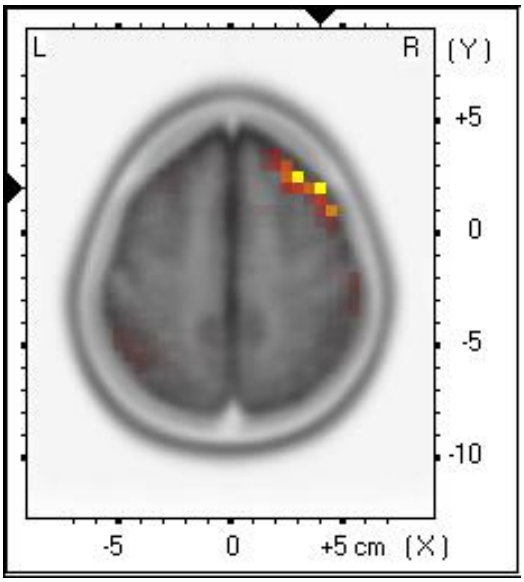
Figure 3.12. Activations observed in Adults (early phase)-superior frontal gyrus, inferior occipital gyrus (late phase)-inferior occipital gyrus. In Adolescents (early phase)-superior frontal gyrus, inferior occipital gyrus (late phase)-superior frontal gyrus.

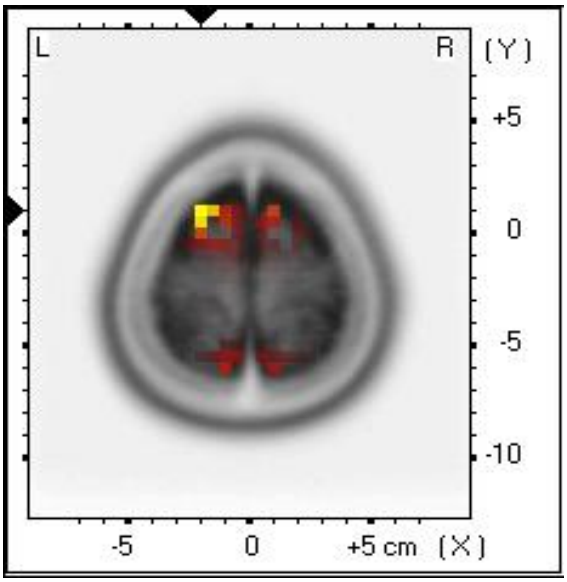
3.13. sLORETTA Images for the early and late delay phases of the Control condition. Rows depict the age groups, and columns depict the phase of the delay period

Early Phase

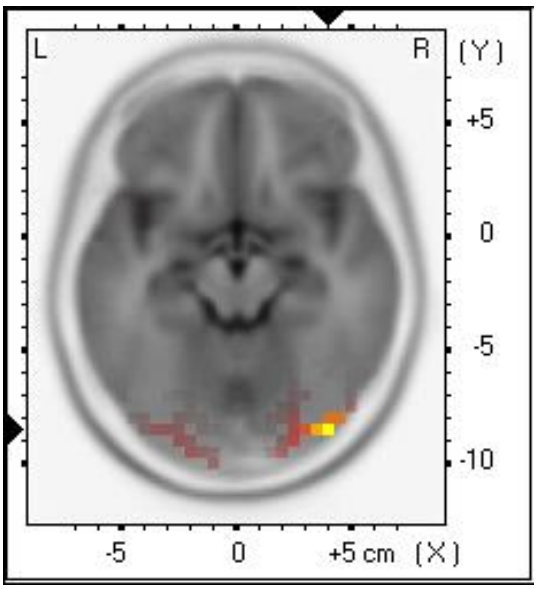
Late phase

Adults





Adolescents



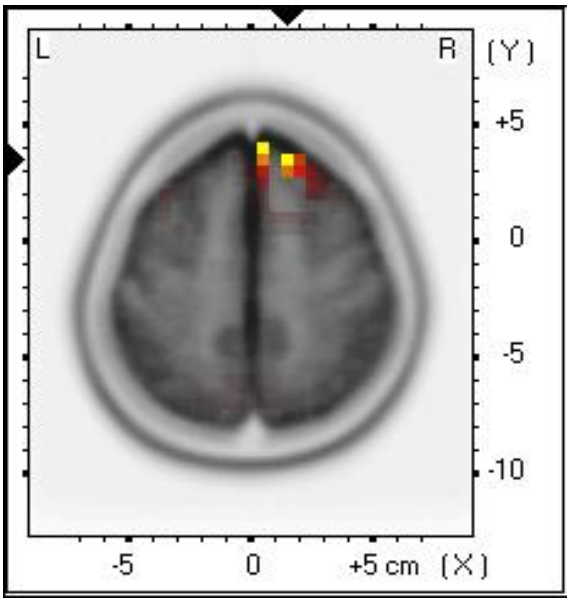


Figure 3.13.Activations observed in Adults (early phase)-superior frontal gyrus (late phase)-superior frontal gyrus. In Adolescents (early phase)-inferior occipital gyrus, (late phase)-superior frontal gyrus.

CHAPTER V

Discussion

The findings of this exploratory study show that neural functioning underlying visual-spatial WM differed between age groups in the Match condition of the ODR tasks, and more specifically this difference was localized anteriorly during the late delay period. Given the protracted maturation of the frontal lobes (Glasser & Easten, 2011), this finding holds developmental significance and the observed variation at the frontal site may indicate that adolescents and young adults may recruit frontal-parietal resources differently. This general finding is supported by research indicating that the circuitry underlying visual-spatial WM, although established during childhood, becomes more refined and specialized throughout adolescence (for example see Geier et al., 2009).

Although several behavioural and cognitive studies show increased capacity and efficiency in WM from childhood to early adulthood (Gathercole, Pickering, Ambridge, & Wearing, 2004; Hamilton, Coates, Heffernan, 2003; Pickering, 2001), there is limited neurophysiological data on the functional maturation of the neural network supporting visual spatial WM especially from adolescence to young adulthood (Klinberg, Forssberg & Westerberg, 2002; Scherf, Sweeney, & Luna, 2006; Thomason et al., 2009). This network connects parietal and frontal regions to support functions of WM, such as sensory and mnemonic processes, as well as response planning and execution of a response (Curtis, Rao, &D'Esposito, 2004; Srimal& Curtis, 2008). Due to the protracted maturation of frontal structures and their connections to more posterior structures, experimental paradigms such as ODR tasks that are shown to activate frontal-parietal regions have been considered valuable tools to investigate visual-spatial WM in relation to brain development (Geier et al., 2009; Luna, Thulborn, Munoz et al, 2001). The main purpose of this

study, therefore, was to explore the possible developmental changes in functional neural networks underlying visual-spatial WM from early adolescence to young adulthood using ODR tasks in conjunction with ERP methodology. This study is unique, as to our knowledge, it is the first developmental study to combine EEG with ODR tasks to explore visual-spatial WM. The EEG methodology was used in this study because high temporal resolution complemented investigation of the precise delay period timing in ODR tasks.

Due to the exploratory nature of this study, no particular hypotheses were generated but two research questions were asked. The first question was related to the age-dependent topographical differences (via Fz / Pz comparisons) in the amplitudes of scalp recorded SW during early and late delay periods of three ODR tasks with different task demands. The second question was related to the age-related differences in neural recruitment during the same time frames (early, late) in the delay periods of three ODR tasks. In contrast to the quantitative approach used to answer the first question, for the second question, source localization of electrical potentials were inspected visually from sLORETA images created from adolescent and young adult data separately, and the resulting images were interpreted rather cautiously in the context of the existing literature.

In the following sections the results pertaining to the first and the second research questions are presented and discussed in light of current findings related to visual-spatial WM development and brain maturation.

Research Question 1: Are there any differences in the SW scalp topography between young adults and adolescents during the early and late delay period of three ODR tasks with varying task demands?

To answer the first question, a mixed ANOVA was conducted with SW area measures during early and late delay periods of Match, Non-match and Control conditions at Fz and Pz electrode sites. The results of this analysis yielded a significant Condition x Electrode Site x Window x Group four way interaction. The three-way ANOVAs per each ODR task revealed significant group main and group interaction effects only in the Match condition. Although in the Control condition, group effect interacted with window and electrode site, the pattern of simple effects were different than the simple effects observed in the Match condition.

Results of the Match condition showed that during both early and late phases of the delay period (see figures 3.6 and 3.7), young adults had larger SW amplitudes compared to adolescents, but this difference was significant only at the frontal midline (Fz) (see figure 3.8). These findings suggest that regardless of the phase of the delay period, anterior-posterior scalp distribution of SW amplitude was significantly different for the young adults (Fz>Pz) but not for the adolescents (Fz = Pz). Moreover, when young adults and adolescents were compared in terms of early versus late delay period activity regardless of the topographical distribution, adults had larger and more positive late delay SW activity (see Figure 3.9).

Overall, during two different phases of the delay period, (early and late), young adults, compared to adolescents showed a distinct topographical distribution. This response was mostly localized anteriorly and almost at the end of the delay period, i.e. 500 ms before the saccade would occur. In other words, more anterior and positive SW was observed in adults during the task that required both retention of the spatial location and the planning of the saccade.

Electrophysiological studies show age-related changes in early and late ERP components (Courchesne, 1978; Friedman, Brown, Vaughan, Cornblatt, & Erlenmeyer-Kimling, 1984) as well as oscilliations in several frequency ranges (Uhlhaas, Roux, Rodriguez, Rotarska-Jagiela,

&Singer, 2010; Segalowitz & Davies, 2004) Research has demonstrated that absolute EEG power is generally lower in young children and adolescents, particularly in slow wave frequency bands (Whitford et al., 2007). Results of developmental ERP research have been interpreted as reflecting both the maturation of brain areas and sophistication of neural network function (Segalowitz & Davies, 2004). Results from the present developmental study indicate that scalp topography and SWs differed between adolescents and young adults during the delay phase of three ODR tasks.

In general, ODR paradigms are used to elicit oculomotor function and visual-spatial WM (Luna et al., 2008). In our paradigm, Match condition required saccade programming and an active retention of visual-spatial information. In consideration of Fuster's (1985) physiological definition of WM, we designed a Match condition to elicit a mediation of multiple brain regions. The neuronal activation pattern observed in the Match condition differed significantly between young adults and adolescents. Young adults demonstrated higher SW amplitude at frontal regions compared to adolescents. A developmental rationale for this difference may be related to task-specific demands of the Match condition.

In comparison to the Non-match and Control conditions, the task demands of the Match condition were more complex. Neuro-imaging research has indicated that task complexity is correlated with an increase in neural activity (Brignani, Bortelleto, Miniussi, & Maioli, 2010; Hamilton et al., 2003; Monfort & Pouthas, 2003). For example, in an EEG study on verbal WM, Monfort and Pouthas (2003) reported an increased amplitude of SW at frontal sites when WM demands increased. fMRI research has demonstrated a higher activation of frontal regions when cognitive load, such as the number of items to retain in memory, increased (Curtis, Rao, &D'Esposito, 2004). Geier et al., (2009) suggest that age-related magnitude differences may

indicate that some aspects of WM are more taxing on the less mature brain. The significant group difference observed in the present study may indicate that Match condition required more complex neural processes, compared to Non-match and Control.

Given the knowledge that increased neural activity may represent how taxing specific task demands are on the developing brain, it is interesting to consider why results of the present study indicate increased activity in adults. The most prominent difference is due to our investigation of the delay period in ODR tasks. Other research that has demonstrated increased activity during adolescence have done so during active periods of memory retention (Hamilton et al., 2003; Monfort & Pouthas, 2003). Since this is one of the few EEG studies to explore brain development in the delay period of ODR tasks, the results need to be interpreted with caution. However, there are a multitude of methodological and developmental reasons for the differences observed in this study.

Temporal vs. Spatial Resolution – The strength of using EEG is its precise temporal resolution. For this reason, results from our study demonstrate when neural activity underlying ODR task performance occurs. The delay period was selected as a time of interest because of its unique properties of persistent SW related to retention of information (Fuster & Alexander, 1971). The SWs examined in the present study were captured in early (700 – 1100 ms) and late (2200 – 2700 ms) time windows. It is interesting that during these precise time periods adolescents presented with a lower magnitude of activity. However, the peak magnitude of the adolescent neural activity may differ from that of adults, and therefore, future analyses will be required to determine what time windows represent peak amplitudes for adolescents during the delay period.

Electode Site. As illustrated in sLORETA images (Figure 3.11), young adults appeared to have more localized activation and adolescents showed a greater dispersion at frontal regions in Match condition. The apriori selection of Fz and Pz electrode sites were based on the long history of research supporting activation of the frontal-parietal network in visual-spatial WM (Fuster& Alexander, 1971; Srimal& Curtis, 2008). However, the 128-channel dense electrode array used in this study provides many sites to explore where young adults and adolescents may show differences in the magnitude of activity across time windows of the delay period. sLORETA.

Development of Network, Recruitment of FEF Structures at Frontal Sites. A third reason may be related to our investigation of the frontal-parietal neural network. Developmental processes involved in network activity affect EEG power (Lüchinger, Michels, Martin, & Brandeis, 2012). Physiologically, neural connectivity and size of neuron populations become more refined throughout maturation (Lüchinger et al., 2012). For this reason, the matured frontal-parietal network may have neural pathways that recruit brain structures differently from adolescents.

Much of the recent literature has investigated the recruitment and function of frontal eye fields (FEFs) in visual-spatial WM (Curtis et al., 2004; Offen, et al., 2010; Postle, 2006).Interestingly, memory performance and target saccade accuracy have been predicted by the magnitude of delay-period activity at FEFs in humans (Curtis et al., 2004; Offen et al., 2006; Scherf et al., 2006). The correlation between increased magnitude and accuracy may indicate a memory storage capacity of the FEFs in humans (Offen et al.). Most importantly, FEFs have demonstrated more activity in ODR delays that require matching of a cue location (Curtis et al., 2004), such as in the Match condition of the present study.

No significant group differences were observed in Non-match and Control conditions. The non-significant group differences in Non-match condition were somewhat surprising given the inhibitory task demands. Neuro-imaging research has demonstrated developmental differences in ODR tasks that require inhibition of a response (Hansell, Wright, Geffen, Geffen, & Martin, 2004; 2004; Luna et al., 2008). Results of these studies have suggested that late maturation of the frontal lobe hinders function of advanced cognitive skills, such as response inhibition, in children and adolescents. The apriori selection of Fz and Pzin the present study may have limited detection of significant group difference sat other electrode sites in Non-match condition.

The non-significant group differences in Control condition were not surprising. The condition was designed to provide baseline measure of frontal-parietal network function. Control condition required basic visually-guided tasks that did not require WM and relied primarily on basic sensory structures. Most ODR research has used Control conditions (Geier et al., 2009; Hansell et al., 2004; Hwang, Velanova& Luna, 2010), similar to the one we used in the present study. The purpose of the Control condition in these studies is to assure the expected activation of frontal-parietal network processes (Geier et al., 2009). For this reason, no between-group differences were expected in the neuronal activation patterns of Control condition.

Research Question 2: Are there differential activations of the neural networks underlying visual-spatial WM between young adults and adolescents during the delay period?

To answer the second question sLORETA images were visually inspected to explore whichbrain regions were most active in early and late windows. Qualitative differences in network activation were observed between age groups at early and late windows. To our knowledge, no other research has used sLORETA to examine source localization in the delay

period of ODR tasks between young adults and adolescents. However,studies have used sLORETAto explore localized activation of brain regions during visual-spatial WM (Brignani, et al., 2010). The activation of frontal-parietal regions observed with sLORETA in the present study aligns with those presented in Brignani et al.'s (2010) research. In the present study, the qualitative interpretation of sLORETA results allow for the visual detection of cortical activation. Figures 3.11-3.13 demonstrate the activation of the parietal and frontal lobes in the early and late phases of delay period activity.

There are several limitations with the sLORETA results presented in this study. The most significant concern is that statistical analyses were not conducted to determine the significance of the regional activations. Secondly, sLORETA uses a model of the entire brain to detect regional sources of activation, and the EEG results presented in this study include only frontal and parietal midline site. For this reason, there are inconsistencies in the interpretation of sLORETA images based upon limited electrode site data. Future statistical analyses will be conducted to determine relevant electrode sites from the full scalp topographical distribution. However, in spite of these limitations, the visual representations indicate that the same network was activated in young adults and adolescents, however, the strength of the network activity varied based on maturation of the brain.

Research question one and two were formulated based on Fuster's physiological definition of WM. According to Fuster, "WM mediates the logical and behavioural cross temporal contingencies between perception and action," (Fuster&Bressler, 2012, p. 211). Mediation of brain regions occur when two or more structures communicate to perform a cognitive function. The mediation of sensory and frontal brain regions observed in the present study signifies the engagement of WM. All three ODR conditions demonstrated activation of the frontal-parietal

network, however, only in the Match condition a statistically significant developmental difference was observed. The fact that this result was detected in the delay period of an ODR task is a unique contribution to better understanding how maturational processes in the brain influence neural functions underlying visual-spatial WM.

Limitations and Future Directions

The contributions of this study need to be considered with its limitations. One of the limitations is the small number of participants in both groups. A larger sample size would have provided greater precision of the averaged EEG data. Future studies will reduce measurement error by increasing sample size, and consequently increase statistical power. However, given the small number of participants, strengths of this research paradigm are apparent in its detection of moderate effect sizes.

A second limitation is the apriori selection of Fz and Pz electrode sites. These sites were chosen because of the expected activation of the frontal-parietal network in visual-spatial WM function. However, exploration of several frontal and parietal scalp sites within the 128-array may have provided a better model to detect significant differences in other electrode sites for Non-match and Control condition, especially since scalp topographies varied in all conditions as a result of neural functions required to complete task-specific demands.

A methodological limitation is the low spatial resolution inherent to EEG technology. Due to this limitation we can only demonstrate an approximation of exact regions that are active in the delay period of ODR tasks. sLORETA was included to strengthen this EEG study, however it was only used as an exploratory tool. Future studies will conduct correlational analyses of sLORETA data to investigate the statistical significance of differences in regional activations between age groups.

Along with advanced statistical analyses, the ODR paradigm will be used in the future to collect data from younger age groups to capture the full developmental trajectory. In addition, the data collected for this study may be used as comparative samples for future investigations with individuals who have clinical diagnoses (i.e., generalized anxiety disorder), learning difficulties or behavioural difficulties (i.e., high impulsivity). All future studies would benefit from an increase in the number of group participants.

Conclusion

This EEG study explored maturation of the visual-spatial WM network. ODR paradigms provided a robust measure to examine neuronal activation patterns in young adults and adolescents during the delay period. Results indicated that the neural activity underlying visual-spatial WM significantly differed at frontal sites during the late (2200 - 2700 ms) window of the delay period. More specifically, results suggested that young adults demonstrated a higher magnitude of frontal activity in the Match condition compared to adolescents. The Match condition required cross-temporal mediation to support WM processes such as active memory retention and saccade planning. In conclusion, results from our study indicate that brain maturation increases the activation of the frontal lobe in the frontal-parietal network subserving visual-spatial WM

References

Asato, R. Terwiilliger, R., Woo, J., & Luna, B. (2010). White matter development in adolescence: A DTI study. *Life Sciences and Medicine*, *20* (9), 2122-2131.

Baddeley, A. (2003). Working memory: Looking back and looking forward. *Nature Reviews Neuroscience*, *4*, 829-839.

Baddeley, A. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences*, *4* (11), 417-423.

Baddeley, A. & Hitch, G. (1974).Working memory. G.H. Bower (Ed.). *The psychology of learning and motivation: Advances in research and theory* (47–89). New York: Academic Press.

Berman, R., Joiner, W., Cavanaugh, J., &Wurtz, R. (2009) Modulation of presaccadic activity in the frontal eye field by the superior colliculus. *Journal of Neurophysiology, 101* (6), 2934-2942.

Brignani, D., Bortelleto, M., Miniussi, C., &Maioli, C. (2010). The when and where of spatial storage in memory-guided saccade.*Neuro Image,* 52, 1611-1620.

Brignani, D., Lepsien, J., Rushworth, M., &Nobre, A. (2009).The timing of neural activity during shifts of spatial attention.*Journal of Cognitive Neuroscience*, *21*(12), 2369-2383.

Bruce C. & Goldberg, M. (1985) Primate frontal eye fields: Single neurons discharging before saccades. *Journal of Neurophysiology*, 53, 603– 635.

Boch, R.A., and Goldberg, M.E. (1989).Participation of prefrontal neurons in the preparation of visually guided eye movements in the rhesus monkey.*Journal of Neurophysiology, 61*, 1064–1084.

Carpenter, R. (1981).Oculomotor procrastination.Fisher, D., Monty, R. & Senders, J. (Eds.).*Eye Movements: Cognition and Visual Perception* (p. 237-246). Hillsdale, NJ: Lawrence Erlbaum.

Constantinidis, C. & Wang, X. (2004).A neural circuit basis for spatial working memory.*The Neuroscientist*, 10, 553 - 565.

Cornoldi, C. &Vecchi, T. (2003).Visuo-spatial working memory and individual differences. New York: Psychology Press.

Courchesne, E. (1978). Neurophysiological correlates of cognitive development: Changes in long latency event related potentials from childhood to adulthood. *Electroencephalography and Clinical Neurophysiology, 45*, 468-482.

Curtis, C., Rao, V, &D'Esposito, M. (2004).Maintenance of spatial and motor codes during oculomotor delayed response tasks.*Journal of Neuroscience*, 24, 3944-3952.

Friedman, D., Brown, C., Vaughan, H.G.,Cornblatt, B., & Erlenmeyer-Kimling, B. (1984). Cognitive brain potentials in adolescents.*Psychophysiology, 21*, 83-96.

Funahshi, S. (2006).Prefrontal cortex and working memory processes. Neuroscience, 139, 251-261.

Fuster, J., & Bressler, S.(2012). Cognit activation: A mechanism enabling temporal integration of working memory. *Trends in Cognitive Neuroscience, 16*, 207-218.

Fuster, J. (1990). Prefrontal cortex and the bridging of temporal gaps in the perception-action cycle. In A Diamond (Ed.) The Development and Neural Bases of Higher Cognitive Functions. New York Academy of Sciences, New York, Vol. 608, p 318-329/

Fuster, J. (1985) The prefrontal cortex, mediator of cross temporal contingincies. *Human Neurobiology*, 4, 169-179.

Fuster, J. & Alexander, G. (1971). Neuron activity related to short-term memory. *Science, 173*, 652-654.

Fuster, J. (1973). Unit activity in prefrontal cortex during delayed-response performance: Neuronal correlates of transient memory. Journal of Neurophysiology, *36*, 61-78.

Gathercole, S.E., Pickering, S.J., Ambridge, B., & Wearing, H. (2004). The structure of working memory from 4 to 15 years of age.*Developmental Psychology,* 2, 177-190.

Geier, C.F., Garver, K., Terwillinger, W., & Luna, B.(2009). Development of Working Memory Maintenance.*Journal of Neurophysiology, 101*, 84-99.

Goldman-Rakic, P.S. (1987).Circuitry of primate prefrontal cortex and regulation of behavior by representational memory.Plum, F. (Ed.), *Handbook of physiology: The Nervous System: Higher Functions of the Brain* (p. 33-68). Bethesda: American Psychological Society.

Grech, R., Cassar, T., Muscat, J., Camilleri, K., Fabri, S., Zervakis, M., Xanthopoulos, P., Sakkalis, V., &Vanrumste, B.(2008). Review on solving the inverse problem in EEG source analysis. *Journal of NeuroEngineering and Rehabilitation****,5*** (25), 5-25.

Hamilton, C., Coates, R., &Heffernan, T. (2003). What develops in visual spatial working memory development. *European Journal of Cognitive Psychology, 15*, 43-69.

Hanes, D. &Wurtz, R. (2001).Interaction of the frontal eye field and superior colliculus for saccade generation.*Journal of Neurophysiology, 85,* 804-815.

Hönegger, C., Attenedera, C., Griesmayr, B., Holz, E., Weber, E. &Sauseng, P. (2011). Neural correlates of visuo-spatial working memory encoding—An EEG study. *Neuroscience Letters*, *500*, 118-122.

Hunter, W. (1913).The delayed reaction in animals and children.*Behavior Monographs*, *2*, 719-743.

Hutton, S. (2008).Cognitive control of saccadic eye movements.*Brain and Cognition*, *68*, 327-340.

Jacobsen, C.F. (1936). Studies of Cerebal Functions in Primates.Baddeley, A., Kopelman, M., & Wilson, B (Eds.).*The Handbook of Memory Disorders* (761-774). New York: Wiley Publishers.

Johnson, M. & de Haan, M. (2011). *Developmental cognitive neuroscience: Third edition*. Massachusetts, USA: Wiley Blackwell.

Jung, R.E., & Haier, R.J. (2007). The parieto-frontal integration theory (P-FIT) of intelligence: converging neuroimaging evidence. *Behavioral and Brain Sciences, 30*, 135-154.

Kemps, E., De Rammelaere, S., &Desmet, T. (2000). The development of working memory: exploring the complementarity of two models. *Journal of Experimental Child Psychology*, *77*, 89–109.

Klinberg, T. (2006).Development of a superior frontal-intraparietal network for visuo- spatial working memory.*Neuropsychologia,44*, 2171-2177.

Klinberg, T., Forssberg, H., & Westerberg, H. (2002).Increased brain activity in frontal and parietal cortex underlies the development of visuo-spatial working memory capacity during childhood. *Journal of Cognitive Neuroscience,14*, 1–10.

Lee, K., &Ahn, K. (2013).The frontal eye fields limit the capacity of visual short-term memory inrhesus monkeys. *Public Library of Science (PLOS) One*, *8*(3), 596-606

Light, G., Williams, L., Minow, F., Sprock, J., Rissling, A., Sharp, R., Swerdlow, N., &Braff, D. (2010). Electroencephalography (EEG) and event-related potentials (ERP's) with human participants.*Current Protocols in Neuroscience*, *6*, 1-24.

Luck, S. (2005). An Introduction to the Event-Related Potential Technique (Cognitive Neuroscience).MIT Press: Cambridge, Massachusetts..

Luna, B., Thulborn, K.R., Munoz, D.P., Merriam, EP., Garver, K.E., Minshew, N.J., Keshavan, M.S.,…Sweeney, S.A. (2001). Maturation of widely distributed brain function subserves cognitive development. *Neuroimage*, *13*, 786-793.

Monfort, V., &Pouthas, V. (2003). Effects of working memory demands on frontal slow waves in time-interval reproduction tasks in humans. *Neuroscience Letters*, *343* (3), 195-199.

Offen, S., Gardner, J., Schluppeck, D., &Heeger, D. (2010).Differential roles for frontal eye fields (FEFs) and intraparietal sulcus (IPS) in visual working memory and visual attention.*Journal of Vision Science*, *10* (11), 1-14.

Pascual-Marqui, R., Esslen, M., Kochi, K., &, Lehmann, D. (2002). Functional imaging with low resolution brain electromagnetic tomography (LORETA): Review, new comparisons, and new validation. *Japanese Journal of Clinical Neurophysiology*, *50*, 81-94.

Pickering, S.J. (2001).The development of visuo-spatial working memory.*Memory, 9*, 423-432.

Postle, B. (2006). Working memory as an emergent property of the mind and brain.*Neuroscience, 139*,23-38.

Scherf, K., Sweeney, J.,& Luna, B.(2006). Brain basis of developmental change in visuospatial working memory.*Journal of Cognitive Neuroscience*, 18 (7), 1045-1058.

Schlag, J. &Schlag-Rey, M. (1985). Unit activity related to spontaneous saccades in frontal dorsomedial cortex of monkey. *Experimental Brain Research*, *58*, 208–211.

Segalowitz, S.J., & Davies, P. (2004).Charting the maturation of the frontal lobe: an electrophysiological strategy.*Brain and Cognition, 55*, 116-133.

Segraves, M. & Park, K. (1993) The relationship of monkey frontal eye field activity to saccade dynamics. *Journal of Neurophysiology*, *69*, 1880 –1889.

Serences, J., Ester, E., Vogel, E.K., &Awh, E. (2009).Stimulus-specific delay activity in human primary visual cortex.*Psychological Science*,*20*, 207-214.

Singh, M., Kim, S., & Singh, T. (2003). Correlation between BOLD-fMRI and EEG signal changes in response to visual stimulus frequency in humans.*Magnetic Resonance in Medicine, 49*, 108-114.

Shah, A. & Miyake, P. (1999). Models of working memory: Mechanisms of active maintenance and executive control. *Cambridge University Press*.

Smith, E., Jonides, J., Marshuetz, C. &Koeppe, R. (1998). Components of verbal working memory: Evidence from neuroimaging. Proceedings of the National Academy of Sciences, 95, 876–882.

Sobotka, S., Dilltz, M.D. &Ringo, J.L.(2005). Can delay period activity explain working memory? *Journal of Neurophysiology, 93,* 128-136.

Sparks, D. & Mays, L. (1990). Signal transformations required for the generation of saccadic eye movements. *Annual Review of Neuroscience, 13*, 309-336.

Srimal, R., & Curtis, C. (2008).Persistent neural activity during the maintenance of spatial position in WM. *NeuroImage,* 39 (1), 455-468.

Tekok-Kilic, A., Tays, W., &Tkach, R. (2011).Activational patterns of the frontal-parietal networks during oculomotor delayed response tasks: An event-related potential study. Poster presented at the 52nd Society for Psychophysiological Research, Boston: MA.

Thomason, M., Race, E., Burrows, B., Whitfield-Gabrieli, S., Glover, G., &Gabrieli, J. (2009). Development of spatial and verbal working memory capacity in the human brain.*Journal of Cognitive Neuroscience*, 21 (2), 316-332.

Tsujimoto, S., &Postle, B.. (2012). The prefrontal cortex and oculomotor delayed response: A reconsideration of the "mnemonic scotoma". *Journal of Cognitive Neuroscience,24* (3), 627 – 635.

Uhlhaas, P., Roux, F., Rodriguez, E., Rotarska-Jagiela, A., & Singer, W.(2010). Neural synchrony and the development of cortical networks.*Cell, 14,* 72-80.

Vecera, R., & Rizzo, M. Spatial attention: Normal processes and their breakdown. *Neurologic Clinics of North America, 21*, 575-607.

Voytek, B. & Knight, R. (2010). Prefrontal cortex and basal ganglia contributions to visual working memory. *Proceedings of the National Academy of Sciences*, 1-41.

Wager, T. & Smith, E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective, & Behavioral Neuroscience*, 3 (4), 255-274.

Wardak, C., Ibos, G., Duhamel, J., & Olivier, E. (2006).Contribution of the monkey frontal eye field to covert visual attention.*The Journal of Neuroscience*, *26* (16), 4228-4235.

Whitford, T.J., Rennie, C. J., Grieve, S.M., Clark, C.R., Gordon, E., & Williams, L.M. (2007). Brain maturation in adolescence: concurrent changes in neuroanatomy and neurophysiology. *Human Brain Mapping, 28*, 228-237.

Zimmer, H. (2008). Visual and spatial working memory: From boxes to networks. *Neuroscience and Biobehavioral Reviews*, *32*, 1373-1395.

Zollig, J., Martin, M., &Kliegel, M. (2010).Forming intentions successfully: Differential compensational mechanisms of adolescents and old adults.*Cortex*, *46*, 575–589.

Appendix A

Developmental Neuroscience Laboratory
Department of Child and Youth Studies
Brock University

CONSENT FORM Date: _____

TITLE OF STUDY: Visual-spatial working memory: What does saccade-related brain activity tell us?

Principal Investigator
Dr.AydaTekok-Kilic
Developmental Neuroscience Lab
Department of Child and Youth Studies
Brock University
(905) 688-5550 ext. 3937
atekokkilic@brocku.ca

M.A Thesis Student
Carleigh Sanderson, M.A. Candidate
Developmental Neuroscience Lab
Department of Psychology
Brock University
(905) 688-5550 ext. 3347

Dear Parent/Guardian:

This form provides you with the information you will need to make an informed decision about whether or not you would like your child to participate in our study on working memory development. Please read it over carefully with your child. The participation is entirely voluntary. If you are interested in participating in our study please contact us at (905) 688-5550 ext. 3937 (Dr.AydaTekok-Kilic), or at (905) 688-5550 ext. 5511 or ext. 3347 (Carleigh Sanderson) to book an appointment. We will only book parents if they initiate contact with us. If you have any questions, you are welcome to phone the researchcoordinator, Carleigh Sanderson, or myself for clarification. We would like to emphasize that the participation is voluntary and we will only book parents if they initiate contact with us.

The goal of the study is to investigate brain function while children, adolescents, and young adults take part in game-like computer tasks. We believe that this study will lead to a richer understanding of how working memory matures.

WHAT IS INVOLVED

The study will take place at the Developmental NeuroscienceLab. You will be asked to come to the lab with your child for a 2 hour session. All of the tasks and procedures will be explained to youand your child. We will review this form with you in the presence of your child so both of you will have a full understanding of what is involved before we begin.

Asoft, elasticized sensor cap is placed on the head to record naturally-occurring brain activity while your child engage in a series of game-like computer tasks. The tasks do not involve motor responding (such as pressing a key) but they involve directing eye gaze to specific locations cued by visual stimuli on a computer screen. Eye gaze is measured by analyzing real-time images taken from two digital cameras attached to the computer monitor. These cameras do not store the images they measure. They only record digitized landmarks that represent participant's eyes and face. It will take about 30 minutes for all of the set-up we require, during which time your child can relax or ask us questions. There will be three 15 minute computer tasks presented sequentially during the study. Including extra time for breaks, the entire session is expected to take 2 hours and there will be a $20.00 honorarium for volunteering your (your child's) time.

POTENTIAL RISKS AND BENEFITS

There are no risks involved in this study. Benefits include introducing participants to research. The techniques and procedures will be fully explained to you and your child. You and your child will be free to ask questions throughout the study. Most participants especially young children find it interesting to see their brain waves and eye tracking on the computer screen. As well, young people often feel good about taking part in a project that could increase our scientific understanding of the factors that influence brain development.

CONFIDENTIALITY

All information gathered is kept completely confidential. Names are replaced with code numbers and it is these code numbers that are entered into our data base along with the physiological information. They will be stored in a controlled-access laboratory, only researchers working on this project will have access to these data and all records of the information will be destroyed when no longer required. Your son or daughter would never be identified in any way when the data are published in academic journals or presented at scientific conferences.

PARTICIPATION IS VOLUNTARY

Participation in this study is entirely voluntary. Either you or your son or daughter may refrain from participating in any component of this study. As well, you or your child may decide to withdraw from this study at any time without penalty even after signing this form.

SECONDARY USE OF THE DATA

The present investigation is designed as a pilot project and therefore the results will be preliminary. The researchers may decide to re-analyze the data in the future. This is considered as "secondary data analyses" and will only be conducted if you give your consent.

CONTACT INFORMATION

If you have any questions about this study or if you would like further information, please contact the project coordinator,Carleigh Sanderson (contact information above). This study has received ethics clearance from the Research Ethics Board of Brock University (#10-211). If you have any comments or concerns about the rights of a research participant, please contact the Research Ethics Office at 905-688-5550, Ext. 3035.

Thank you for considering this project. If you would like your child to participate, please return a signed copy to the lab in the envelope provided but keep the extra copy for your records.

CONSENT

I agree on behalf of myself and with the assent of my child to participate in the study described above. I have made this decision based on the information provided above and have had the opportunity to receive any further details and understand that I am welcome to ask any further questions in the future. I also understand that I can withdraw this consent at any time without penalty even after signing this form.

Parent/Guardian's Name: _____

Signature: _____ Date: _____

Child's Name: _____

Signature: _____ Date: _____

I also agree on the secondary use of the data collected for this research by the researchers in future research.

Parent's Signature: _____ Child's Signature: _____

Appendix B

Developmental Neuroscience Laboratory
Department of Child and Youth Studies
Brock University

CONSENT FORM Date: _____

TITLE OF STUDY: Visual-spatial working memory: What does saccade-related brain activity tell us?

Principal Investigator
Dr.AydaTekok-Kilic
Developmental Neuroscience Lab
Department of Child and Youth Studies
Brock University
(905) 688-5550 ext. 3937
atekokkilic@brocku.ca

M.A, Student
Carleigh Sanderson, M.A. Candidate
Developmental Neuroscience Lab
Department of Psychology
Brock University
(905) 688-5550 ext. 3347

Dear Participant:

This form provides you with the information you will need to make an informed decision about whether or not you would like to participate in our study on working memory development. Please read it over carefully and if you have any questions, you are welcome to phone the researchcoordinator, Carleigh Sanderson (905) 688-5550 ext. 3347 or, or myself (Dr A. Tekok-Kilic) at ext. 3937 for clarification.

The goal of this study is to investigate brain function while participants take part in game-like computer tasks. We believe that this study will lead to a richer understanding of the brain mechanisms underlying the functionality of working memory processes and its development.

WHAT IS INVOLVED

The study will take place at the Developmental NeuroscienceLab. You will be asked to come to the lab for a 2 hour session. All of the tasks and procedures will be explained to you and we will review this letter with you so you have a full understanding of what is involved before we begin.

Asoft, elasticized sensor cap is placed on the head to record naturally-occurring brain activity while you engage in a series of game-like computer tasks. The tasks do not involve motor responding (such as pressing a key) but they involve directing eye gaze to specific locations cued by visual stimuli on a computer screen. Eye gaze is measured by analyzing real-time images taken from two digital cameras attached to the computer monitor. These cameras do not store the images they measure. They only record digitized landmarks that represent your eyes and face. It will take about 30 minutes for all of the set-up we require, during which time you can relax or ask us questions. There will be three 15 minute computer tasks presented sequentially during the study. Including extra time for breaks, the entire session is expected to take 2hours and there will be a $20.00 honorarium for volunteering your time.

POTENTIAL RISKS AND BENEFITS

There are no risks involved in this study. Benefits include introducing participants to research. The techniques and procedures will be fully explained to you and you will be free to ask questions throughout. Most participants find it interesting to see their brain waves and eye tracking on the computer screen. As well, young people often feel good about taking part in a project that could increase our scientific understanding of the factors that influence brain development.

CONFIDENTIALITY

All information gathered is kept completely confidential. Names are replaced with code numbers and it is these code numbers that are entered into our data base along with the physiological information. They will be stored in a restricted-access laboratory, only researchers working on this project will have access to these data and all records of the information will be destroyed when no longer required. You would never be identified in any way when the data are published in academic journals or presented at scientific conferences.

PARTICIPATION IS VOLUNTARY

Participation in this study is entirely voluntary. You may refrain from participating in any component of this study. As well, you may decide to withdraw from this study at any time without penalty even after signing this form.

SECONDARY USE OF THE DATA

The present investigation is designed as a pilot project and therefore the results will be preliminary. The researchers may decide to re-analyze the data in the future. This is considered as "secondary data analyses" and will only be conducted if you give your consent.

CONTACT INFORMATION

If you have any questions about this study or if you would like further information, please contact the project coordinator,Carleigh Sanderson (contact information above). This study has received ethics clearance from the Research Ethics Board of Brock University (#10-211). If you have any comments or concerns about the rights of a research participant, please contact the Research Ethics Office at 905-688-5550, Ext. 3035.

Thank you for considering this project. If you would like to participate, please return a signed copy to the lab in the envelope provided but keep the extra copy for your records.

CONSENT

I agree to participate in the study described above. I have made this decision based on the information provided above and have had the opportunity to receive any further details and understand that I am welcome to ask any further questions in the future. I also understand that I can withdraw this consent at any time without penalty even after signing this form.

Participant's Name: _____

Signature: _____ Date: _____

I also agree on the secondary use of the data collected for this research by the researchers in future research.

Participant's Signature: _____

This participant received research participation hours (___) or an honorarium (___).

Appendix C
TELEPHONE SCRIPT – For Undergraduate Volunteers

Name _____ Phone _____

Thank you for calling. My name is _____. Let me first tell you about the study. We are interested in how thebrain supports performance on tasks requiring attention and memory. We are studying brain and cognitive development as humans grow and change from young children into adults. We would like you to come to the Developmental Neuroscience Lab at Brock University for a single 2 hour session. During this session, you will complete 3 versions of a computerized memory task in the form of a game while we use EEG to monitor your naturally occurring brain response and visual sensors to monitor the direction of your eye movements.

Of course, we will explain all procedures to you fully when you arrive at the lab before you begin. But I can answer any general question you might have right now (give any practical or technical information required). If you think you might be interested, can I ask you a few health-related questions to see if the study would be appropriate for you. Is this alright? This and all other information is kept strictly confidential.

1. What is your birth date? _____ Approx years of education?_____ Right or left-handed? _____
2. Do you have any visual problems? _____ Yes No
4. Do you have any major health conditions? _____ Yes No
6. Do you have any conditions that could affect nervous system function? Yes No
(e.g., multiple sclerosis, epilepsy, fibromyalgia?)
7. Do you have diabetes, 82ypoglycaemia, lupus, chronic fatigue syndrome? Yes No
8. Have you ever had any serious psychiatric difficulties? Yes No
(e.g. diagnosed ADD, clinical depression___, other?_____)
9. Have you ever had a head injury or concussion? If yes:_____ Yes No

If serious visual problems, or serious physical, neural or mental condition say.....
Having _____ could affect the physiological responses that we will be measuring so I'm afraid that this study won't be appropriate for you . However, if you are still interested, we could send you some information about the outcome of the study when it's ready. Also, there may be other studies coming up where _____ would not be an issue. If you like, I can put your name on a list and we could contact you about participating at another time.

If health screening is passed say: That all seems fine. However, since we will be collecting EEG, there are a couple of other things I have to ask: Do you use non-permanent hair dye? ____ Is your hair extremely thick? _____ In corn rolls? ____ Dreadlocks? _____ Anything else that might make fitting a tightly fitting cap difficult?
Would it be alright for you to not wear makeup (or remove any makeup) the day you come for the study?

If they meet criteria and are willing to participate …
o Take contact info, arrange an appointment, and describe how to get to the lab.
O If they wear contacts, suggest wearing glasses that day instead.
O Remind them that this is entirely voluntary and that they are free to withdraw at any time if they wish.
O Tell them that we can email or call to give a reminder prior to their visit.
O THANK THEM!

Contact Information:

Appointment Date:

Appendix D
Developmental Neuroscience Lab, Brock University
Feedback Form

Project Title: Visual spatial working memory: What does saccade-related brain activity tell us?

Dear Participant,

Thank you for taking part in this study. Without the help of volunteers like you, this research would not be possible.

As you know we measured EEG and monitored your eye-movements while you completed very simple computer games that required you to maintain specific spatial locations in mind. Holding or manipulating information in your mind over a short period of time is referred to as "working memory" and is fundamental to both basic and complex thinking in human beings. In this study, we are specifically interested in how children and young adults are able to hold spatial information in working memory and use that knowledge to properly guide the eyes to the locations required in our computer game.

The working memory functions you needed to use in this study are supported by various regions of the brain including the dorsolateral prefrontal cortex and frontal eye fields (both in the front of the brain) as well as the inferior parietal lobule (located about several centimetres behind and above your ears). Understanding how these different areas support the storage of spatial information and are used to guide the movement of your eyes is of great interest to cognitive neuroscientists. By recording brain responses in children of various ages, we can chart the development of the different neural structures involved in spatial working memory and the control eye movements. This information can also be used to identify and understand abnormal developmental trajectories in spatial working memory as well how damage to the brain (from head injuries or disease) can be expected to impact mental skills and behaviour.

As you are aware from the consent form, all of your data will be kept strictly confidential and when the data is presented, you will not be identified in any way.

If you would like to learn more about the results of this study, feel free to contact the principle investigator (see below). However, please be advised that it takes several months to complete data collection and then to process the data and perform necessary analyses. Thus, preliminary results are not likely to be ready before the summer of 2011.

If you have any issues that you would like to discuss regarding your involvement in this study, you may contact the Brock Research Ethics Board through the Research Office at 905-688-5550, Ext: 3035, File # 10-211.
Thank you again for taking part in this study. Your help was very much appreciated.

Principle Investigator:
Dr.AydaTekok-Kilic
atekokkilic@*brocku.ca*
Lab Phone: 905-688-5550, Ext: 3347
Office Phone: 905-688-5550, Ext: 3937

APPENDIX E

Example of ODR Task Paradigm